ANAEMIA IN CHILDREN.

A study of its manifestations, causation, treatment and prognosis with notes of cases.

by

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October, 1928.

Thesis for the Degree of M.D.

I N D E X.

SECTION I.

INTRODUCTION.

Anaemia is a clinical picture frequently encountered among all classes at all ages. It is the immediate cause of indisposition in a large proportion of a doctor's patients. While in adults the indisposition usually amounts to an inability to carry out the day's work, in children the effects are far more extensive and serious.

The tissues and organs of the growing child require for their proper and progressive development an abundant supply of the end productions of digestion. An adequate supply of these end products can only be maintained if the blood is normal in both its cellular and fluid constituents. In anaemia, by reason of the profound alterations in the cellular constituents with perhaps lesser alterations in the fluid constituents of the blood, the growing, developing tissues are no longer supplied with an adequate amount of such end products. There is as a direct result hypoactivity of many tissues and organs and a risk of permanent defects of development.

This thesis deals with anaemia as it affects infants and children.

Certain signs and symptoms are generally accepted as/

as indications of the presence of anaemia. I have enquired into the nature and frequency of the various aetiological factors, the various lines of treatment and the value of the various signs as prognostic indications. I have examined the blood cells in a series of children, healthy and unhealthy, and have endeavoured to find some relation between these findings and the clinical manifestations.

DEFINITION.

To define anaemia from a clinical point of view is difficult and also unsatisfactory, for all the symptoms and signs which in various combinations constitute the generally accepted clinical picture of anaemia, may each be due to causes other than anaemia.

Anaemia may be defined from a clinical point of view as the condition which arises when from some cause or causes a combination of several of the following symptoms and signs are present.

Symptoms.

A feeling of lassitude and weakness, sometimes associated with irritability and restlessness.

A tendency to fainting associated with giddiness.

A feeling of numbness and tingling in the extremities.

Signs./

Signs.

Examination reveals:-

Pallor.

Rapidity of pulse rate and a lowering of blood pressure.

Enlargement of the heart and displacement of the apex beat.

The presence of murmurs over the heart and in the neck.

A "wateriness" of the blood as it issues from a wound.

Anaemia may be defined from the laboratory point of view as the condition which arises when from some cause or causes the composition of the blood as regards its corpuscular and haemoglobin content is altered so as to be lower than certain accepted standards, e.g. in an adult male when it falls below 5,000,000 red corpuscles per c.mm. with a haemoglobin content less than 90 per cent.

The number of corpuscles varies with age, therefore before one can diagnose anaemia in a given case, one must have some definite standards of comparison. To arrive at such standards blood examinations have been carried out on a number of healthy children, consisting in an enumeration of the red blood corpuscles, the white blood corpuscles, an estimation of the haemoglobin, determination of the colour index, examination of stained films, and a differential count of the white blood corpuscles.

METHOD.

The practical work of this thesis consists almost entirely of blood examinations. The methods adopted are those usually carried out in the Royal Infirmary, Edinburgh.

The lobe of the ear, or in infants the heel, was cleansed with ether and pricked with a needle, or vaccinostyle, and the first drop of blood wiped away. The red counting pipette was then filled up to the .5 mark, wiped clean, and the diluting fluid drawn up to the 101 mark, shaken and laid aside. The white counting pipette was similarly filled up to .5 mark then diluting fluid drawn in up to the 11 mark, shaken and laid aside.

The next drop was used for the estimation of haemoglobin. In most cases Tallqvist's paper scale was used. The reading was taken just after the gloss had disappeared, and allowance made for the fact that the standard of this scale is based on von Fleischl's haemoglobinometer in which the normal is 90 per cent. The results obtained by Tallqvist's paper were accordingly written down - 10 per cent.[1]

Tallqvist's scale was used on account of the relative simplicity of the determination, and with the full knowledge that there is a considerable margin of error.

In some of the cases the haemoglobin content was estimated by Dare's Haemoglobinometer.

In/

Two films were made on slides.

The cells were usually counted within four hours from the time of taking the specimen.

The red counting pipette was shaken thoroughly and a few drops of the diluted blood were expelled. A drop was then run in over the cover slip of a Thoma's Haemacytometer. After a few minutes the slide was placed under the 1/6th objective and the cells lying within the area of 5 sets of 16 small squares were enumerated, 80 in all, and the count repeated using another drop of diluted blood.

The sum of the figures for each 5 sets of 16 small squares multiplied by 10,000 gives the results per c.mm. for, where:-

X is the total number of cells.
1/4000 the volume of one small square in c.mms.
200 the degree of dilution.
and 80 the number of small squares counted, the number of cells in 1 c.mm. will be

$$\frac{X \times 4000 \times 200}{80} \quad \text{or} \quad X \times 10,000$$

The average of two such readings was taken.

The white cells lying within the area of the whole set of 400 small squares were enumerated under the 2/3rds objective. The fine adjustment was moved up and down to bring into focus any cells which had not settled on to the surface of the counting chamber. The leucocyte count was repeated five times.

The/

The figure obtained multiplied by 200 gives the result per c.mm. for

where

X is the total number of cells
1/4000 the volume of one small square in c.mms.
20 the degree of dilution.
and 400 the number of small squares counted,

the number of cells in 1 c.mm. will be

$$\frac{X \times 4000 \times 20}{400} \quad \text{or} \quad X \times 200.$$

The average of the five readings was calculated.

Differential count.

Films were stained by Jenner's method, undiluted stain covering the dried film for 1 to 1½ mins., an equal quantity of distilled water was added and the diluted stain allowed to act for 3 to 6 mins. The films were then washed in distilled water and dried with filter paper.

100 white cells were counted on each of two films and the results expressed as a percentage.

The Colour Index was determined by dividing the percentage haemoglobin by the percentage number of red corpuscles as compared with blood containing 5,000,000 per c.mm., or the figure for the haemoglobin divided by twice the first two digits of the red count, e.g.,

R.B.C.s. 4,500,000 or 90 per cent.

Hb. 80 per cent.

Colour Index is .88.

GROUPS.

Since children vary somewhat in the rate of growth and development the writer is of the opinion that a more useful purpose would be served by placing the children in groups delineated by outstanding events than by placing them in groups strictly determined by age.

Group I. Birth to beginning of 1st dentition.

II. To the completion of 1st dentition.

III. To the time of going to school.

As there is no outstanding event in development between time of going to school and puberty, this period has been divided according to age:-

Group IV. To the age of 7½ years.

V. To the age of puberty.

RESULTS.

Blood examinations were carried out on 55 children who were presumed to be healthy, i.e., at time of the examination there were no evidences of septic infections, enlargement of the tonsils or other conditions likely to alter the results.

TABLE I./

TABLE I.

No.	Sex.	Age	Grp.	R.B.Cs.*	W.B.Cs.	Hb.	C.I.	Differential. P.	SL.	LL.	E.	B.	T.	M.	NRs.
1	M	7.6	V	4,330	8,650	80	.91	49	31	13	2.5	1.5	2	1	-
2	M	8.7	V	4,890	7,360	80	.83	63	21	10	2	-	2.5	1.5	-
3	F	7.9	V	4,610	8,600	75	.81	47	38	10	1.5	-	2	1.5	-
4	F	6.7	IV	4,610	8,120	70	.76	52	30	11	3	-	2.5	1.5	-
5	M	4.3	III	4,680	11,280	70	.75	36	49	9	2	-	3	1	-
6	F	1.0	II	5,210	9,880	65	.62	29	57	8.5	1.5	-	2.5	1.5	-
7	M	.6	I	4,920	15,050	80	.81	22	59	11	2	-	5	1	-
8	M	1.1	II	5,290	10,700	60	.57	35	48	12	1	-	2	2	-
9	M	6.1	IV	4,680	9,050	70	.76	56	29	8	2	1	1	3	-
10	F	2.7	III	4,940	10,050	65	.66	47	39	8	2	-	2	2	-
11	F	3.1	III	4,880	9,240	65	.68	44	40	9	3	-	2.5	1.5	-
12	M	6.6	IV	4,790	7,600	75	.61	38	42	11	2	-	4	3	-
13	M	3.5	III	4,650	10,120	65	.69	48	35	12	-	-	4	1	-
14	M	5.3	IV	4,570	7,840	75	.83	56	29	8	-	1	3	3	-
15	M	6.5	IV	4,650	8,580	70	.75	51	26	15	1	1	4	2	-
16	F	.5	I	5,150	16,840	85	.83	35	46	14.5	1	-	2	1.5	-
17	M	3.2	III	4,740	10,480	65	.67	45	40	9	2.5	-	3	1.5	-
18	F	10.9	V	4,590	8,950	70	.77	59	23	10	2	.5	3	2.5	-

* R.B.Cs in thousands.

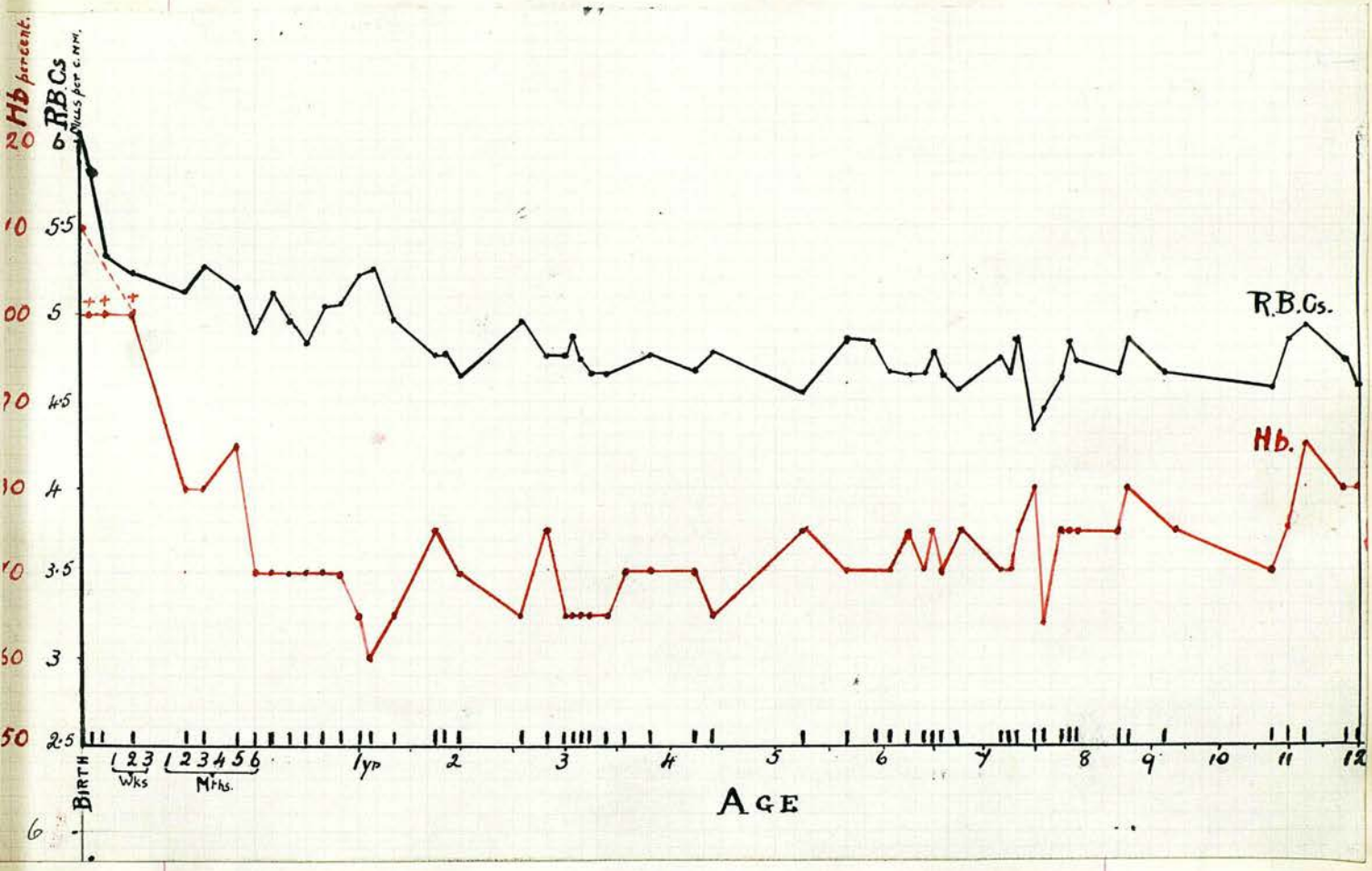
									Differential.					
No.	Sex	Age	Grp.	R.B.Cs.	W.B.Cs.	Hb.	C.I.	P.	SL.	LL.	E.	B.	T.	M.	NRs.
19	M	.3	I	5,300	11,600	80	.75	22	61	10	1.5	.5	4	1	-
20	M	7.7	V	4,460	6,150	65	.73	48	38	9	2.5	.5	1.5	.5	-
21	F	7.2	V	4,720	7,320	70	.74	64	19	10.5	2	.5	2.5	1.5	-
22	F	12.0	V	4,580	6,750	80	.88	49	28	12.5	1.5	-	4	5	-
23	M	11.10	V	4,710	8,050	80	.85	52	27	11	3	-	3	4	-
24	F	9.2	V	4,670	9,560	75	.80	51	30	11	2	1	2.5	2.5	-
25	M	2/52	I	5,230	13,120	100+	.98	36	39	13	6	1	3.	2	-
26	M	.7	I	5,150	10,400	70	.67	28	52	11	2.5	-	2.5	4	-
27	F	8.6	V	4,650	9,800	75	.79	69	22	5	1	.5	1.5	1	-
28	M	2.0	II	4,620	11,900	70	.76	28	48	16.5	2.5	1.5	1	2.5	-
29	F	.11	I	5,090	14,450	70	.70	30	48	12	3	.5	2.5	4	-
30	M	11.3	V	4,920	10,600	85	.86	42	37	14	4	-	2	1	-
31	M	2/365	I	5,810	21,100	100+	.94	67	18	8	1	1	2	3	3 MY 2
32	F	7.3	V	4,690	10,900	70	.76	65	24	5	1.5	5	2	2	-
33	F	3.7	III	4,790	10,920	70	.75	54	30	10	1	-	2.5	2.5	-
34	M	4/365	I	5,310	18,300	100	.94	56	21	10	2.5	1.5	6	3	2
35	F	.2	I	5,160	12,640	80	.77	29	55	10	1	-	4	1	-
36	F	5.8	IV	4,840	8,440	70	.73	46	34	9	4	.5	2.5	4	-
37	M	6.9	IV	4,570	10,240	75	.83	64	25	4	2	-	2	3	-

								Differential.								
No.	Sex.	Age	Grp.	R.B.Cs.	W.B.Cs.	Hb.	C.I.	P.	SL.	LL.	E.	B.	T.	M.	NRs.	
38	M	3.10	III	4,790	11,800	70	.75	57	28	8	2	.5	2.5	2	-	
39	M	2.10	III	4,780	12,400	75	.79	51	34	8	1.5	.5	3.5	2.5	-	
40	F	3.3	III	4,640	10,720	65	.71	38	42	11	3.5	-	1.5	4	-	
41	M	7.4	V	4,860	7,440	75	.77	64	22	6	1.5	.5	3	3	-	
42	M	3.0	III	4,710	9,150	65	.70	47	39	16	2	1.5	3	1.5	-	
43	F	7.10	V	4,840	8,550	75	.78	56	26	9	2	-	3	4	-	
44	M	.9	II	4,820	10,950	70	.73	26	60	7	2	1	2	2	-	
45	M	7.11	V	4,710	9,600	75	.79	54	27	11	1.5	1	2.5	3	-	
46	F	.8	II	4,980	10,160	70	.71	33	51	8	3	-	2	1	-	
47	F	4.5	III	4,790	9,720	65	.70	39	38	10	3.5	1.5	3	5	-	
48	F	.10	II	5,060	11,040	70	.70	35	50	8	1.5	-	3.5	2	-	
49	M	3.8	III	4,620	9,640	65	.71	45	36	8	4	-	3.5	3.5	-	
50	F	N.B.	I	6,190	17,450	110	.91	60	21	8	1	-	5	5	5	ǂ
51	M	1.4	II	4,060	11,750	65	.66	56	25	9	1	-	4	5	-	ǂ
52	M	1.10	II	4,790	9,800	75	.78	48	38	6	3	1	1.5	2.5	-	ǂ
53	M	6.3	IV	4,640	8,680	75	.81	57	24	9	3	1	3	3	-	
54	F	11.0	V	4,830	8,760	75	.78	67	18	7	2	-	3	3		ǂ
55	M	5.11	IV	4,860	8,100	70	.73	47	34	11	2.5	-	3	2.5		ǂ

50 N.B:= Newly born child. ǂ Haemoglobin estimated by Dare's haemoglobinometer.

Graph I shows the curve of the number of red corpuscles and of the percentage of haemoglobin in the above series of cases.

GRAPH I.



From the results given above it was found that the average figures for the various groups given on page were as follows:-

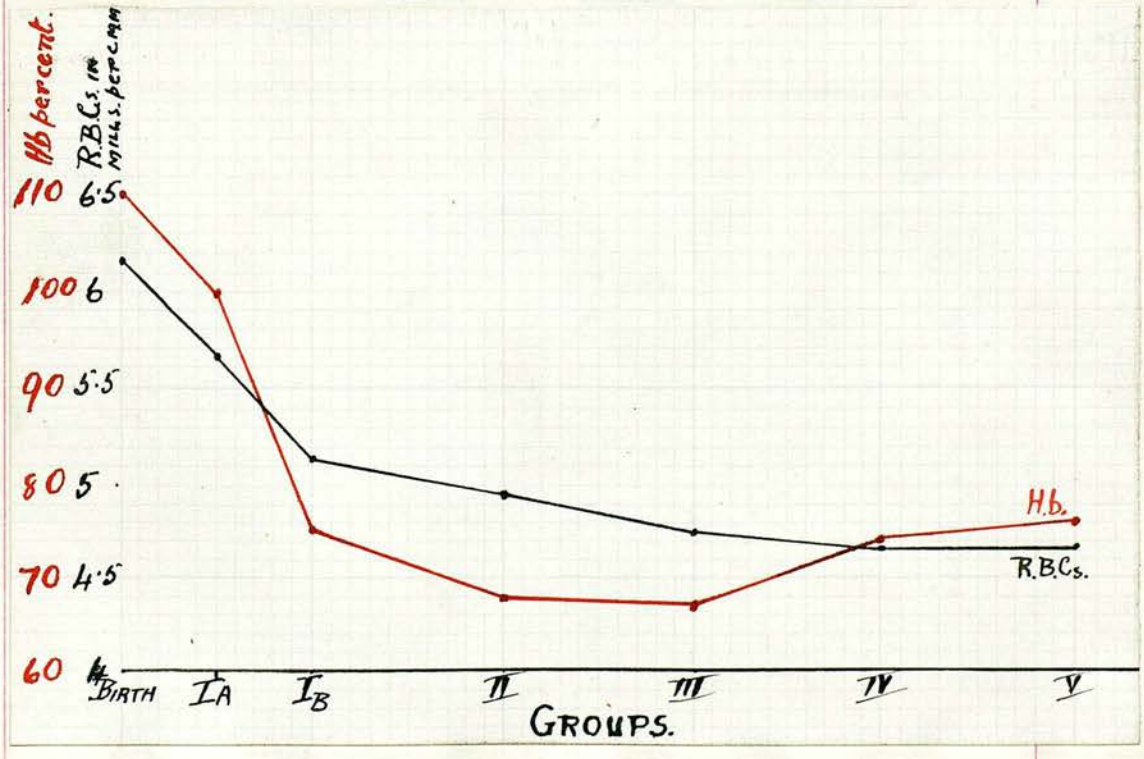
Note:- Group I was subdivided into IA from birth to 2nd week and IB, 2nd week to commencement of 1st dentition, since the blood picture during the first two/

two weeks differed very markedly from the picture during the remainder of the period included in group I.

	R.B.C.s	Hb.
Group IA	5,640,000	100 +
IB	56,130,000	76
II	4,967,000	68
III	4,750,000	67
IV	4,670,000	72
V	4,682,000	76

Graph II shows the average number of red corpuscles and percentage haemoglobin for the various groups.

GRAPH II.

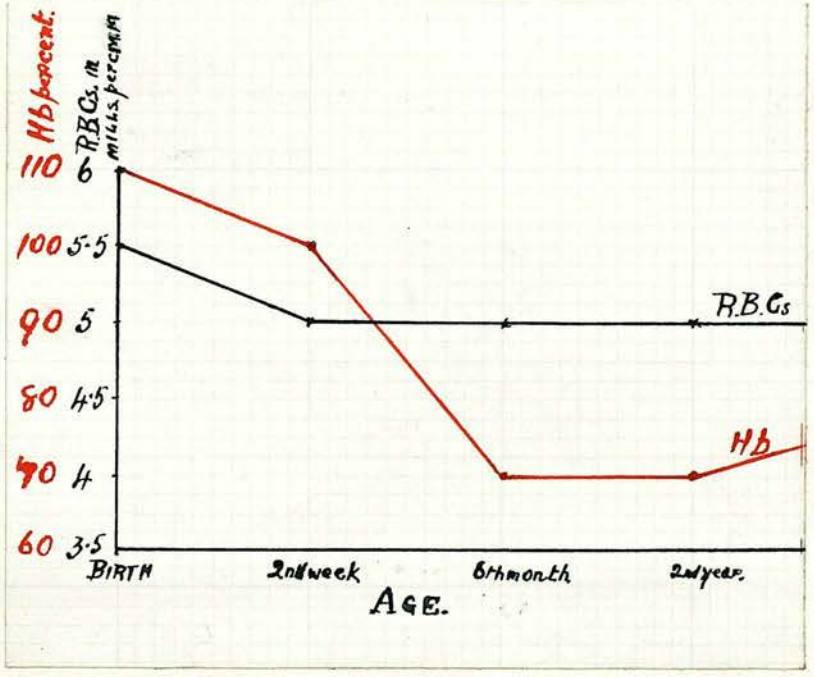


DISCUSSION.

There is a divergence of opinion among the various authors as to what constitutes the normal blood count at various ages.

Hutchison gives the following table.[2]

GRAPH III.



Gulland places the figure for red corpuscles at birth at 6 millions with 120 per cent haemoglobin rapidly falling to normal (i.e. 5 millions) within 2 weeks while the haemoglobin continues to fall down to 80 per cent at 10 years and rising again to 100 at 12 years.[3]

Thomson gives rather lower figures and states that/

that the haemoglobin falls to 70 per cent at 6 months, rising again to 90 per cent at 6 years[4].

Morse gives the following figures:-

	R.B.C's.	Hb.
Birth	6 - 7½ mills.	120 per cent.
2 weeks	5½-6 mills.	-
3 months	-	60 per cent.
6 years	5 mills.	70 per cent.
13 years	5 mills.	80 per cent [5]

Griffiths&Mitchell state that the number of red corpuscles falls from 5½ millions at birth to 5 millions in the 2nd week and to 4½ millions during infancy.

Lucas gives a less detailed and much wider range of figures.

Red corpuscles during 1st week 5 - 7 millions with haemoglobin 120 - 100 per cent.

Red Corpuscles during infancy and childhood 4 - 4½ millions with haemoglobin 80 - 95 per cent [6]

Anaemia is essentially a condition affecting the number of red blood corpuscles and their content of haemoglobin but in any blood examination to determine the presence or absence of such a condition and in arriving at any conclusion as to the cause or the state of the haematopoietic tissues cognisance must be taken of the numbers and characteristics of the white corpuscles. Since the white cells of the granulocytic/

granulocytic series are formed in the red bone marrow coincidently with the red corpuscles, they will show parallel alterations and since they are more highly differentiated cells such alterations can be more readily detected by microscopic methods.

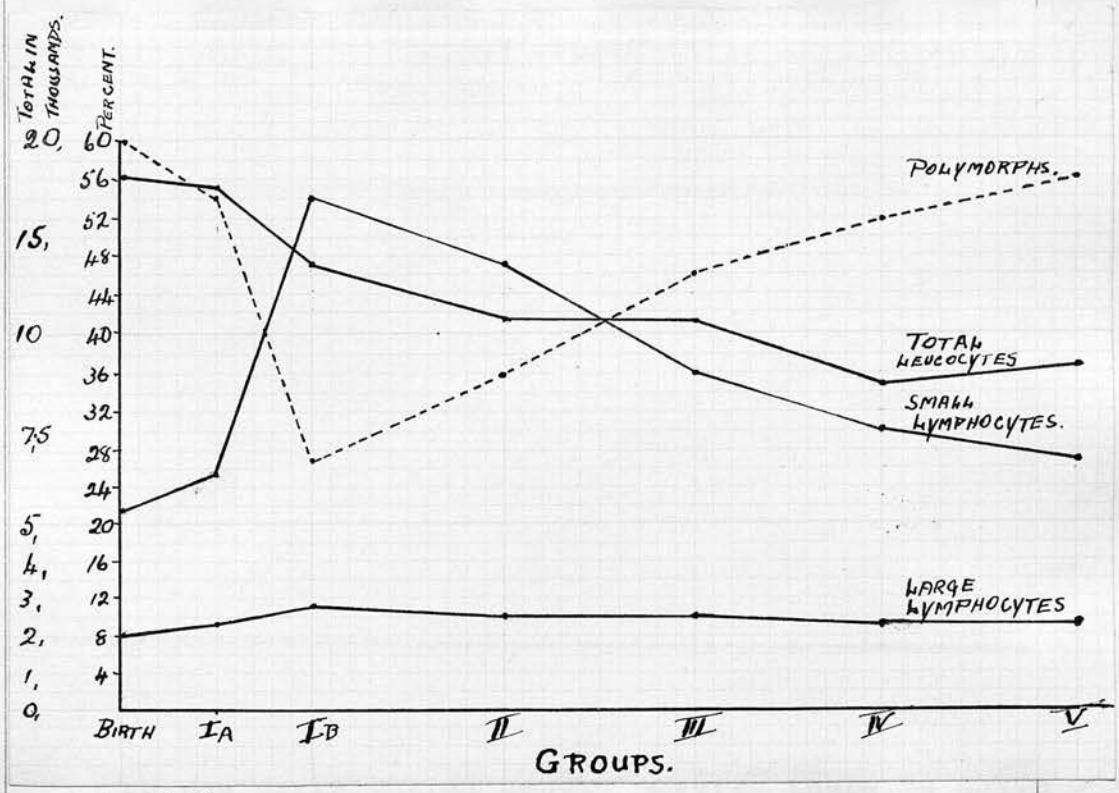
A detailed examination of the white cells in the form of a differential count and in special cases a "Schilling Index" will be of the utmost value.

From the above series of cases the total average number of white cells per c.mm. and the percentage of the various types of cells in the groups were as follows:-

		Differential.						
Group.	Total W.B.C's	P.	SL.	LL.	E.	B.	T.	M.
IA	17,500	55	25	9	2.5	1	4	3.5
IB	13,490	27	54	11	2	.5	3.5	2
II	10,690	36	47	10	2	.5	2.5	2
III	10,460	46	36	10	2	.5	3	2.5
IV.	8,570	52	30	9.5	2	.5	3	3
V.	9,220	56	27	9.5	2	.5	2.5	2.5

Graph IV shows the curve of the number of leucocytes and the percentages of the various types of cells for the groups.

GRAPH IV.



DISCUSSION.

The figures given by various authors for the variations with age in the white cell count correspond more closely than do the figures for the red cell count although the latter is much more stable and less liable to variations from relatively small stimuli.

Hutchison gives the following table which, if taken as showing the upper limit, would include the figures/

figures given by Gulland, Morse, Thomson, Griffiths and Mitchell and Lucas.[7]

GRAPH V.

In the differential counts however there is again a divergence of opinion as is shown in the tables given below.

		Polymorphs.
Gulland.	Birth	60 per cent.
	10 days	55 per cent.
	1 year	30 per cent. rising throughout childhood to the adult 50 per cent.[8]

		Polymorphs.
Morse.	Birth	35-40 per cent.

Griffiths-Mitchell.

Polymorphs.

1st year	30 per cent.
2nd year	30 per cent.
6th year	45 per cent.
10th year	55 per cent.
13th year	65 per cent.[9]

The writer's results correspond to the figures given by Gulland, Griffiths and Mitchell.

In addition to the numerical variations discussed above, variations in the appearance of the red cells were noted.

The films of the newly born showed numerous polychromasic cells and a number of normoblasts. Normoblasts were present on the 2nd day but were fewer in number and only a few polychromasic cells were found.

Nucleated red cells were present on the 4th day but no polychromasia was found.

A Schilling Index[10] of newly born child gave

Myelocytes	1 per cent.	Total Neutrophil leucocytes 61 per cent.
Metamyelocytes	9 per cent.	
Polymorphs	51 per cent.	

SUMMARY.

The number of red cells per cubic millimetre at birth is high, with a relatively high percentage of haemoglobin.

The number of red cells falls rapidly and is lowest at the end of Group I, the percentage haemoglobin continues to fall into Group IV, thereafter the percentage rises gradually into adult life.

The number of red cells throughout infancy and childhood is less than 5 million.

The percentage haemoglobin shows considerable variations but is always below 80 per cent throughout infancy and early childhood.

The writer did not find any outstanding variations between the counts in the sexes.

The white cells are very numerous at birth with a high percentage of polymorphs. The total number falls rapidly during the first two weeks and thereafter continues to fall less rapidly until the adult figure is reached in Group V.

The percentage of polymorphs falls rapidly during the first two weeks, continues at this level through Groups I and II and then rises to adult figures.

The percentage of lymphocytes is relatively high from the second week up to end of Group II.
There is an increase in the number of immature forms of granulocytes at birth, thereafter the number corresponds closely to the adult figure, i.e. about 4 per cent.[11]

SECTION II.

CLINICAL MANIFESTATIONS.

The manifestations of anaemia may be the first indication that a child is ill, but on the other hand these are frequently super-imposed on the manifestations of another disease, e.g. in acute rheumatic fever.

The symptoms and signs vary somewhat according to age of the child.

In infants of Group I there are no real symptoms, but the mother notices a progressive increase in pallor and listlessness. The child appears very feeble and may even be unable to suckle properly, leading to a failure to gain weight normally. In severe cases the mother may notice swelling of the extremities.

In Group II the manifestations are similar to the above, and since splenic anaemia (Von Jaksch's disease) occurs typically in this Group, swelling of the abdomen is sometimes noticed by the mother.

In Group III the child is disinclined for play, is peevish and very often constipated. The child is easily tired out and does not take its food well.

In Groups IV and V the symptoms are more definite. The child complains of tiredness, giddiness and even of/

of fainting. The patient is unable to compete with his playmates and becomes discouraged and introspective.

Turning to the examination of a well-developed case of anaemia in a child of the later groups, the first thing observed is the creamy pallor of the complexion with an almost hectic pink flush of the malar regions in some cases. The palpebral conjunctivae, lips and gums are pale. The child is usually moderately well developed. The whole appearance suggests lassitude and lack of interest. Oedema may be present in infants with a severe degree of anaemia.

SYSTEMS.

Circulatory.

Pulse rate is accelerated, the wave is small and easily compressible. The apex beat may be visible through the thin chest wall as a diffuse pulsation below the nipple line in the sixth intercostal space. Pulsations are also visible at root of neck and in the epigastrium.

Palpation confirms the displacement of the apex beat outwards, no thrill can be detected.

Auscultation. The 1st sound is soft and may be prolonged. Soft blowing systolic murmurs over the pulmonary, aortic and mitral areas, loudest over the pulmonary, louder on lying down and well heard at the side of the vertebral column behind are frequently present./

present.

The 2nd sound is soft and unaccentuated.

A venous hum, "bruit de diable" is sometimes audible over the lower part of the external jugular vein just above the medial end of the clavicle.

Veins. These are sometimes dilated and prominent especially in cases of anaemia associated with rickets or general debility in infancy.[12]

The extremities are cold to the touch.

Haemopoietic.

The spleen is sometimes enlarged and palpable below the costal margin. The lymphatic glands are often slightly enlarged.

Blood count.

R.B.C's	about	2,500,000
W.B.C's	"	20,000
Hb.	"	30 per cent.
C.I.	"	.6.

Film:- There is marked achromia of the red corpuscles which show as mere rings of pink instead of the normal well formed discs.

Anisocytosis and poikilocytosis are present and also nucleated red cells in severe cases.

Polychromasia of the red cells may be present.

A polymorphic leucocytosis is frequently present.

Digestive./

Digestive.

Appetite is poor and the bowels confined. The lips are pale. The tongue is pale, thin and moist. The abdomen is sometimes protuberent, with enlargement of the liver and spleen and there is sometimes flatulent distension.

Respiratory.

There are seldom any signs directly referable to anaemia.

Nervous.

The child complains of noises in the ears and giddiness, is irritable and fretful and lacks power of concentration. There may be fainting attacks.

The reflexes and sensations are seldom altered.

SECTION III.

AETIOLOGY.

The production of anaemia depends on:-

I. Alterations in the number of the cells circulating in the blood.

II. Alterations in the quality of the cells circulating in the blood.

I. The number of cells circulating in the blood stream depends on the balance struck between two opposing factors.

1. Rate of production.
2. Rate of destruction.

Anaemia results when the rate of production is slowed, when the rate of destruction is accelerated or when both are accelerated, the rate of destruction being accelerated to a greater extent than the rate of production.

It is seldom possible to state with a degree of certainty which of these factors is present in a given case.

A slowing of rate of production alone is shown in some cases of congenital anaemia where the child is pale from birth, does not respond to treatment, and dies in six weeks to two months. Clinically these cases resemble the aplastic anaemia of adults. There are/

are no evidences of increased destruction, e.g., enlargement of spleen; jaundice or increase of urobilin in the urine.

An acceleration of the rate of destruction alone is well shown in malaria, where the number of red corpuscles falls rapidly at the time of sporulation. There are no evidences that the rate of production is slowed for nucleated reds appear in numbers corresponding to the degree of anaemia.

Blood formation.

In post natal life the chief seat of blood formation is the red bone marrow. Subsidiary seats are the spleen, liver and lymph glands. In the red or formative marrow the various cells of the erythrocytic and granulocytic series are developed. It is noticeable that in children the red marrow entirely fills the cavities of all the bones, whereas in the adult it fills the cavities in the short and flat bones and only the extremities of the cavities of the long bones.

The formative marrow is made up of a network of fibrous tissue, finer blood vessels and sinusoids inset with islands of fat and haematopoietic tissue. The blood supply reaches the cavity by the nutrient artery which divides into the branches running in the network and ends in sinusoids lined by flattened endothelial cells. These endothelial cells form part of a special/

special tissue known as the "reticulo-endothelial system" which has recently been shown to play an important part in haematopoiesis.

Various theories have been given to explain the method by which the newly formed cells enter the blood stream. One theory suggests that the walls of the sinuses are incomplete and that the cells pass directly into the blood stream. Other theories suggest that the cells have the power of permeating the endothelial walls and give the findings in inflammation as evidence where the red cells are found in great numbers around the site of infection while no break in the vessel walls can be found.

The various types of cells found in a stained preparation of active bone marrow will now be described briefly.

Megakaryocytes - very large cells with multiple nuclei and acidophil cytoplasm containing oxyphil and azurophil granules.

Haemocytoblasts - large rounded and somewhat ill-defined cells with clear faintly basophil staining cytoplasm and a feebly staining basophil nucleus.

Megaloblasts - large cells about 20 microns in diameter, faintly acidophil cytoplasm containing a small amount of haemoglobin. The nucleus is vesicular and/

and basophil.

Normoblasts - very numerous cells about 8-10 microns in diameter with acidophil cytoplasm and intensely staining basophil, round, central nucleus whose chromatin has a radial arrangement resembling spokes of a wheel.

Normocytes - circular acidophil cells without nuclear structure.

Myeloblasts - frequently large cells 12-16 microns in diameter with faintly basophil clear cytoplasm and relatively large round nucleus faintly basophil in reaction showing in its chromatin network 2-6 nucleoli.

Pre-myelocytes - smaller than the myeloblast with cytoplasm containing numerous small neutrophil granules, the nucleus shows four small nucleoli.

Myelocytes - distinguished by their definitely granular cytoplasm and relatively large palely basophil indented nucleus. These cells are of three kinds according as the granules stain eosinophil, basophil or neutrophil.

Polymorphonuclear leucocytes - with faintly acidophil cytoplasm, numerous granules and characteristic relatively small, deeply basophil, multilobulated nucleus. The granules are of three reactions as in the myelocytes.

Basophil polymorphs are smaller as a rule and the nucleus does not stain so deeply.

Eosinophil polymorphs are larger than the neutrophils with a palely staining nucleus often bilobar, the two rounded lobes being joined by a fine chromatin thread.

Small lymphocytes only a little larger than the normocyte, with a narrow ring of clear basophil cytoplasm and a relatively large intensely staining round nucleus.

Large lymphocyte about twice as large as the above with similar staining reactions but relatively greater amount of cytoplasm.

Transitionals - large cells with staining reactions of the lymphocytes distinguished by an indented or kidney shaped nucleus. A few granuloid bodies may be present in the cytoplasm which finer methods have shown to be aggregations at the junctions of the reticular threads.

Large mononuclears or monocytes - still larger with clear faintly basophil cytoplasm and rounded basophil nucleus. Resembles the myeloblast somewhat but the internal structure of the nuclei differ, that of the monocyte having more clearly outlined chromatin particles which aggregate at the periphery to form a darker area resembling a membrane, the nucleoli are smaller.[13]

In/

In a stained section of bone marrow by far the most frequent cells are the granular leucocytes, chiefly neutrophil myelocytes and polymorphonuclears. There are fairly numerous islets of normoblasts and occasional groups of megaloblasts.

This tendency for the various cells to occur in groups has been very well brought out by examination of sections from rabbits made anaemic by injections of ricin etc. Such work has thrown considerable light on the relationship of the various cells to one another. On the assumption that in a group or islet, the younger cells are found in the centre and more mature forms at the periphery, it would appear from such sections that in post-natal life megaloblasts do not as a rule give rise to normoblasts. In the majority of islets of normoblasts no megaloblast is found and no normoblasts are found around the islets of megaloblasts.[14]

The relationship of the various cells is a subject of controversy among haematological experts. The most undifferentiated marrow cell, the haemocytoblast probably gives rise to the various cells of the erythrocytic and granulocytic series, while a similar cell in the lymph glands and spleen gives rise to cells of the lymphatic series.

Recent work has shown the monocytes to be derived from the reticulo-endothelial system.

The routine production of the elements found in the healthy circulating blood appears to be carried on by the division of the myelocytes and normoblasts. The less frequent and earlier cells, e.g., myeloblasts and megaloblasts, seem to exist only to renew the vigour of this stock from time to time and to increase its number when great necessity arises. These "parent" cells themselves can be formed from the simple cell of the reticulo-endothelial system, the histiocyte, if further calls are made on the haemo-poietic system.

Piney is of the opinion that the histiocyte can form either leucocyte or normocyte according as to whether the development is extra or intra vascular, also that when the histiocyte responds to a demand for an increased output of one type, it cannot at the same time produce the normal number of the other.

Blood Destruction:-

The cells of the blood especially the non-nucleated erythrocytes have a definite "life", estimated at from 3-6 weeks. It has now been proved that cells which are damaged or effete, are destroyed in the spleen, liver and haemo-lymph glands, for in haemolytic jaundice, where there is intense haemolysis, the removal of the spleen leads to a great diminution in this process and disappearance of the symptoms, although/

although the abnormality of the red blood corpuscles persists.[15]

One of the functions of the spleen is to filter the blood flowing through its sinusoids, removing by a process of selection, organisms, foreign particles and effete or damaged blood cells. This function is vested in the cells of the reticulo-endothelial system, which can be demonstrated in sections of various organs by their property of taking up any foreign particles injected into the blood stream, e.g., Indian Ink. Normally such cells in the spleen contain partially broken down red corpuscles.

The cellular structure of the erythrocyte is destroyed after ingestion and the constituents of the cytoplasm pass by the splenic vein to the liver. Fragmentation of erythrocytes in the blood stream also takes place.[16]

Phagocytosis of the erythrocytes by the polymorpho-nuclear leucocytes has been observed in cases of congenital anaemia with jaundice.[17]

The lipoprotein part of the corpuscle is stored in the liver. The iron containing part is dealt with by the Kupffer cells of the liver which are recognised as part of the reticulo-endothelial system.

White corpuscles. Effete and damaged white cells are dealt with in a similar manner by the spleen.

This/

This is shown in myelogenous leukaemia, where such a process may reasonably be expected to be exaggerated, by finding, in sections of the spleen, cells of the reticulo-endothelial system containing the nuclei of leucocytes in process of disintegration.[18] A dead leucocyte is the ordinary "pus corpuscle", characterised by its faintly staining cytoplasm, often vacuolated with very few granules and small pyknotic nucleus.

AETIOLOGY II.

The quality of the cells circulating in the blood may be altered so as to produce anaemia.

In certain cases of anaemia the number of corpuscles is practically normal while each contains an amount of haemoglobin much less than normal, e.g., chlorosis, where the percentage haemoglobin may fall to 40 per cent or less.

Haemoglobin is a very complex substance and from the known facts regarding the absorption of iron, one of its most important constituents, and proteins in general, it must be built up from very simple "stones". The seat of this process is probably the liver.

The process of destruction of haemoglobin is more definitely known. After lysis of the corpuscles in the spleen the haemoglobin passes unaltered or only very slightly so, to the liver. The first step in the splitting up is the separation of the protein fraction Globin, the remaining iron-containing fraction is Haematin. Haematin is further split up into Haemosiderin, which contains iron, and Haematoidin which is the source of the bile pigment, Bilirubin.[19] Haemosiderin is stored in the liver in small quantities and presumably used in the elaboration of new haemo-globin. An excess of Haemosiderin in the liver is shown/

shown by an intense Prussian blue reaction, e.g., in Pernicious Anaemia where excessive blood destruction is going on.

In view of the extreme complexity of Haemoglobin, its elaboration is likely to be very easily deranged and the effects of a decrease in this very important metabolic substance to be frequently met with, i.e., anaemia.

SECTION IV.

PATHOLOGY.

This section deals with the alterations in the appearances of the blood cells found in stained preparations, the significance of these changes and the post-mortem findings.

In a film stained by Jenner's method the following alterations in the cells are found.-

1. There is alteration in the staining reaction of the red corpuscles, all the cells are paler than normal, achromia , some cells take up an excess of the blue stain, polychromasia, others show numerous fine dark granules, punctate basophilia.
2. There is irregularity in the size of the red corpuscles, anisocytosis. When the cells are smaller than normal they are known as microcytes, when larger as macrocytes or megalocytes.
3. There is alteration in the shape of the red corpuscles, poikilocytosis, many cells are pyriform, crescentic or irregular in outline.
4. Nucleated red corpuscles are found, either normoblasts or megaloblasts.
5. No alteration can be detected in the cells of the lymphocytic series.

6./

6. In the granulocytic series however many changes are noted. The neutrophil polymorphonuclear cells show an increase in less differentiated forms, i.e., cells with "bandshaped" or bilobar nuclei. The occurrence of myelocytes, and a shift to the left of the Ahrneth count. The nuclei may be deeply stained or pyknotic and the cytoplasm may be palely stained and vacuolated.

In a film stained by one of the finer methods, e.g., Cunningham's vital staining, additional changes are noted.

Vital staining is a process of allowing a drop of blood to come into contact with a fine deposit of brilliant cresyl blue on a cover slip or slide, making a smear and staining by Jenner's method.

Normal blood stained by this method shows a reticulation of fine blue threads in about 1 per cent of the red corpuscles.

7. An increase in the number of reticulated red cells.
8. The occurrence of Cabot rings and Howell-Jolly bodies in the red corpuscles.

The significance of these various alterations has been the subject of much discussion.

The alterations in size and shape are to be considered as evidences of an excessively hurried regeneration.[20]

Polychromasia/

Polychromasia is a sign of immaturity of the red corpuscles and so an evidence of active regeneration.[21]

Punctate basophilia, which is rare in childhood, is a sign of degeneration.[22]

The presence of nucleated red cells is an indication of increased activity of the bone marrow.

Increase in the number of reticulated red cells is an evidence of active regeneration for, in acholuric jaundice after a haemolytic crisis the percentage may rise to 30.[23]

Increase in the number of "band" polymorphs is an evidence of bone marrow activity.

Pyknosis and vacuolation are evidences of degeneration.

The evidences of <u>active regeneration</u> may be summarised.

The occurrence of:-

1. Anisocytosis with macrocytosis.
2. Nucleated red cells.
3. Polychromasia.
4. Cells with Cabot rings and Howell-Jolly bodies.
5. An increase in number of reticulated red cells.
6. An increase in number of "band" polymorphs.
7. An increase in the number of blood platelets.[24]

The evidences of <u>defective regeneration</u> may be summarised:-

The/

The occurrence of:-

1. Paleness of red cells (achromasia)
2. Shadow red cells.
3. Punctate basophilia.
4. Microcytosis and perhaps poikilocytosis.
5. Crenation of red cells.
6. Vacuolation and pyknosis of the polymorphs.

POST-MORTEM FINDINGS.

At the sectio pallor of the organs is a marked feature.

Thorax. Only the heart shows changes due to the anaemia per se, usually a fatty degeneration of the muscle fibres, best seen in the "thrush breast" heart in pernicious anaemia and diphtheria.

Abdomen. The liver may be slightly enlarged and may show a few small haemorrhages on its surface. It may also show fatty degeneration. The spleen is often enlarged, the Malpighian bodies are unaltered to the naked eye. The kidneys occasionally show a fatty degeneration. The bone marrow is very little altered in children.

All these findings are very variable and depend on the cause of the anaemia and on the cause of death.

Microscopic examination of the liver shows a slight degree of fatty degeneration and in some cases a deposit of haemosiderin in the liver cells.

In/

In the spleen there are evidences of increased activity of the reticuloendothelial cells. Immature types of red and white cells may be present.

The changes in the organs can be accounted for by three factors.

1. The fatty changes in the organs occur partly on account of the incomplete metabolism resulting from the deficient oxygen carrying capacity of the blood, also as a result of the action of a toxin which is at the same time the cause of the anaemia.

2. The presence of immature cells in the organs are due to these organs taking up again the functions of blood formation which they performed in ante-natal life, i.e. myeloid metaplasia.[25]

3. The increased activity of the reticulo-endothelial cells of the spleen and the deposition of haemosiderin in the liver are due to the increase in the number of damaged cells in the circulation which have to be dealt with.

SECTION V.

CLASSIFICATION.

Anaemia may be classified under three headings:-

1. Congenital.
2. Primary.
3. Secondary.

1. Congenital includes cases where from soon after birth there is a degree of anaemia.

2. Primary at present includes cases where the function of maintaining the blood supply is directly attacked, for which no definite cause can be discovered.

3. Secondary anaemias are those commonly encountered, a cause or causes can be found and the removal of these where possible leads to a restoration of the normal blood picture.

CONGENITAL.

Cases are described by various authors of anaemia from birth with jaundice. The writer has never observed such a case. The features are anaemia of a severe degree, jaundice of moderate degree, progressive enlargement of the liver and spleen, bile stained urine and clay coloured stools.

The blood shows a decrease in the number of erythrocytes/

erythrocytes and a lowering of the percentage of haemoglobin which is relatively greater. A degree of leucocytosis with relative increase in the polymorphs.[26]

Many of these cases end fatally, a few recover.[27]

Cases are also described of well marked anaemia arising a few days after birth without jaundice which rapidly recover.[28]

PRIMARY.

Von Jaksch's anaemia or anaemia pseudo-leukaemia infantum is a clearly cut blood disease in children. It is usually regarded as a primary anaemia although by some authors it has been regarded as a secondary anaemia following on rickets or congenital syphilis from its co-existance with these diseases. Most probably the relationship is due to these separate diseases being most frequently found under the same hygienic conditions in children of the same age.

The disease arises in children of both sexes, rather more frequently in boys between the ages of six months and two years. The outstanding signs and symptoms are, the creamy, waxy pallor of the skin and mucous membranes, loss of flesh and digestive disturbances.

Examination shows a protuberant abdomen with considerable enlargement of the spleen and liver, occasionally/

occasionally the presence of ascites. The spleen is smooth, hard, sharp-edged and without tenderness. It may reach down to the umbilicus. Cardiac murmurs are present. A few lymph glands may be palpable in the groins or neck.

The blood shows diminution in number of erythrocytes with low percentage haemoglobin so that the colour index is considerably below unity. White corpuscles are always increased in numbers, a marked leucocytosis involving all types, there is a relative increase in polymorphs and many immature cells (myelocytes) are present. In a film the red cells show marked anisocytosis with large numbers of nucleated forms, polychromasia and punctate basophil may be present.

These cases respond to treatment almost invariably, and recover in two or three months, although the enlargement of the spleen may persist for a much longer time.[29]

The causation of the anaemia is obscure. The association with rickets suggests a metabolic factor, the regularity with which the disease appears in children of the same age suggests an hereditary defect in the blood forming organs. It is plain that the spleen is not primarily at fault since the alteration in size shows no constant relationship to the anaemia. Digestive upset and hygienic conditions play a small part.

PERNICIOUS ANAEMIA.

Occasionally occurs in children when the signs, symptoms, blood changes and pathology are similar to those of the disease in the adult and will not be described.

The causation of the anaemia has been the subject of much discussion. Most authorities agree that the ultimate cause is a toxin although they differ in their views as to its origin. Hunter finds the toxin in infective conditions of the tongue, teeth and bowel associated with achlorhydria. Toxin of bacillus Welchii in the duodenum has been put forward as a cause. Other authorities regard the condition as a primary disease of the bone marrow. The most modern work seems to point to some primary defect in the liver functions for treatment with extracts of that organ has given very spectacular results. (Minot and Murphy.)

The effects of these various causes is to increase the rate of blood destruction and to stimulate the blood forming organs in a peculiar manner. Very marked increase in haemolysis is shown by the mild jaundice and deposits of haemosiderin in the liver. There are also all the evidences of active regeneration, normoblasts, megaloblasts, polychromasia etc, in stained films.

Whether the anaemia is due to the relatively greater/

greater increase in blood destruction, or to the fact that the hyperplastic bone marrow is unable to produce normal corpuscles, has not been decided. Evidence in proof of this latter theory is found in the presence of large numbers of myelocytes in the bone marrow while there is a marked reduction in the number of fully developed polymorphonuclear leucocytes in the circulating blood. The megaloblasts in the marrow share in the hyperplasia hence the occurrence of these cells also numerous megalocytes in the circulating blood. This constitutes a reversion to the foetal type of blood formation.

Anaemia Gravis or Aplastic Anaemia[30] is a disease in which there is progressive diminution in the number of red corpuscles, white corpuscles and amount of haemoglobin.

In spite of the very marked anaemia a stained film has a surprisingly normal appearance. There is complete absence of signs of regeneration in the circulating blood and the marrow, no anisocytosis, poikilocytosis nor nucleated red corpuscles.

The blood formative tissues are either inherently weak or are completely overwhelmed by some toxin. The result is invariably fatal.

Does/

Does secondary anaemia ever become primary? Using the definitions of primary and secondary anaemia given on page 40 this cannot occur, but from time to time cases are noted in which from some definite cause an anaemia develops showing the characteristics of pernicious anaemia, the most widely accepted of the primary anaemias, e.g., in Borthiocephalatus latus infections and further any secondary anaemia may become aplastic showing that such diseases cannot be sharply divided into distinct classes.

SECONDARY.

The causes of secondary anaemia may be arranged in tabular form thus:-

PHYSICAL:	Haemorrhage	Rapid, from a wound.
		Slow, in Haemophilia and Purpura Haemorrhagica.
	Increased fragility of the red corpuscles, in Family Acholuric Jaundice.	
TOXIC:	Bacterial,	Chronic suppurations, Tuberculosis, Rheumatic fever, Congenital syphilis, Nephritis, Diphtheria, Scarlet fever, etc.
	Chemical,	Lead poisoning.
PROTOZOAL:	Direct,	Malaria
	Indirect,	Intestinal parasites.

NEOPLASTIC:/

NEOPLASTIC:	Intrinsic,	Leukaemias, Chloroma, Hodgkin's disease, Gaucher's disease, Status lymphaticus,
	Extrinsic,	Carcinoma Sarcoma,
METABOLIC:	Early,	Rickets, Infantile scurvy,
	Late,	Intestinal indigestion, Endocrine deficiencies.
HYGIENIC:	Defective ventilation, " sunlight, " clothing, etc.	

A more detailed examination of the mode of action of these various causes is necessary.

PHYSICAL.

When a rapid haemorrhage occurs either externally as from a wound, or internally as in rupture of the liver, there is decrease in the total volume of the circulating blood, a loss of both cellular and fluid elements. The volume of the fluid element tends to be restored quickly by passage of plasma from the tissue spaces into the blood vessels by a process of osmosis. This process continues at a progressively slowing rate until the volume of the circulating blood is restored to normal, a period which usually extends from 24 to 36 hrs.

Since, however, there is no corresponding reserve of blood corpuscles their number per c.mm. is less quickly restored. Immediately after a haemorrhage the/

the number will be unaltered. During the next 24 hrs. there is a progressive diminution in the number of red corpuscles and an increase in the number of white corpuscles for the latter are swept into the blood stream with the flow of plasma from the tissue spaces and from the active bone marrow.

The red corpuscles may be affected by the altered osmotic pressure of the plasma, they take up moisture and become swollen. Some of the cells, nearing the end of their period of usefulness, will be unable to accommodate themselves to the changes. Such cells break up, further reducing the number.

After 36 hrs., when the volume of the blood has been restored, active regeneration commences and the number of red corpuscles increases steadily. At first a few normoblasts are seen in films. This may be in an attempt to carry on blood formation in the splenic sinusoids or may be due to the cells having been extruded from the bone marrow before their development had been completed.

Rapidity in rate of production is also shown by abnormal staining reactions of the red corpuscles, the presence of small cells, of polychromasic cells and occasionally immature white corpuscles. The percentage of haemoglobin is relatively lower, for the tendency is to restore the number of cells first and the quality later, probably since the elaboration of haemoglobin is/

is a more complex process.

The leucocytosis involves all types with a relative increase in the polymorphonuclear neutrophils.

SLOW HAEMORRHAGE.

The typical example of anaemia following on continuous small loss of blood is that of gastric ulcer. Two conditions give somewhat similar results in children.

Haemophilia, in which there is an inherent slowing and diminution in the coagulability of the blood, gives rise to oft repeated small losses of blood. Haemorrhage from any wound, no matter how trivial is severe and prolonged. Such children who survive infancy and learn to walk, are exposed to a great variety of scratches and knocks each of which leads to a loss of blood either externally or as ecchymoses or haemarthroses, with the production of anaemia. It is remarkable that the needle prick made in taking samples seldom causes prolonged bleeding.[31]

The blood shows a slight decrease in number of red corpuscles with greater drop in percentage of haemoglobin as if in these cases from repeated stimulation the bone marrow is ready and able to supply the required corpuscles quickly but the manufacture of haemoglobin has not been correspondingly accelerated.

Purpuras, as a whole and Purpura Haemorrhagica in particular,/

particular, from the characteristic petechial eruptions and in the latter from the haemorrhages from the nose, bowel etc. cause anaemia. Purpura Haemorrhagica is comparatively common. The blood shows certain well-marked changed, typical of secondary anaemia, of a degree varying with the amount of blood lost. There is lengthening of the bleeding time, diminution in the number of blood platelets and non-retraction of the blood clot. Why the repeated haemorrhages of these diseases do not lead to the very severe degree of anaemia as do those from gastric ulcer in the adult is probably because in the latter there is always a toxic or infective element present. In purpura haemorrhagica the physical loss of blood may not be the only cause of anaemia, for it may reasonably be supposed that the agent which acts on the capillary walls in such a way as to cause their rupture may also exert an injurious action on the red blood corpuscles.

INCREASED FRAGILITY of the red blood corpuscles.

This condition which is best known in acholuric family jaundice, gives rise to a varying degree of anaemia, the number of red corpuscles may fall to 2,000,000 per c.mm. or less with haemoglobin relatively lower, even to 30 per cent in a severe case.[32] The blood picture shows an increase in the number of microcytes, /

microcytes, marked anisocytosis, polychromasia and punctate basophilia with a few neucleated red cells.

The fragility of the red corpuscles is determined by setting up a series of small test tubes containing 3-5 ccs. of various dilutions of salt solution, .9 per cent to .3 per cent by gradations of .05 per cent. A quantity of a suspension of centrifuged blood corpuscles equal to the amount of saline in the tube is added. After mixing, the results are determined at the end of one hour by observing in which tubes the tinging of the fluid with red ceases. Normally this takes place in the tube containing .4 per cent saline, in acholuric family jaundice it occurs at a strength of .6 or .7 per cent.[33]

In addition to anaemia in this disease there is persistent mild jaundice which is due to the number of red corpuscles destroyed being so great that the Kupffer cells of the liver cannot cope with the amount of haemoglobin brought to them from the spleen. Some bile passes through the liver, hence the stools are not pale and there is no bile in the urine. Enlargement of the spleen is almost invariably present in an effort to deal with the increase in the amount of work it has to do.

TOXIC.

BACTERIAL. The part played by bacteria and their toxins in the production of anaemia is very large. Practically every organism which is pathogenic to man can cause a degree of anaemia. The Pyogenic organisms are very frequently the cause of anaemia as is well shown in empyema and prolonged suppuration following osteomyelitis. The detailed mechanism of causation in these cases is rather difficult to determine. The chief factor is undoubtedly a toxic substance of unknown chemical constitution which is absorbed from the site of infection and acts either directly on the corpuscles producing haemolysis or on the bone marrow interfering with its function of blood formation.

Direct action on the blood corpuscles is well shown in the case of infection by certain strains of streptococci where their property of lysing blood "in vitro" is used to differentiate them. The exact nature of this haemolysis has not been elucidated but most probably the toxin unites with or acts upon one of the constituents of the capsule of the red corpuscle, e.g., lecithin, giving rise to rupture and escape of the haemoglobin into the blood plasma. This toxin also acts indirectly by interfering with normal process of blood formation in the marrow through its/

its haemolytic action on the forerunners of the red corpuscles.

Another factor present is the increase in the number of white corpuscles which invariably follows any infection with a pyogenic organism. These corpuscles which form the defensive mechanism of the body, congegrate at the site of infection and by ingesting the organisms, attempt to render them innocuous.

Since these cells are formed for the most part in the bone marrow, their increase, in response to the infection, reduces the space available for the development of red corpuscles. Further, since both red and white corpuscles are developed from a common ancestor, the excessive production of one type may lead to a lessened production of the other.

A third factor is the swinging temperature which interferes directly with blood formation. Pyrexia upsets the metabolism and so reduces the amount of material available for blood formation.

TUBERCULOSIS, no matter which organ or tissue it attacks, is constantly accompanied by a degree of anaemia.

Affecting the lungs, the degree is usually slight or moderate.

When in an infection of the bones and joints, abscesses/

abscesses form, rupture and leave sinuses, the degree of anaemia becomes much more marked from the action of the toxins of the secondary infecting organisms.

In abdominal tuberculosis, especially when the Peyer's patches are involved to the extent of ulceration, the factor of imperfect digestion and absorption is added. The irritable bowel tends to hurry the contents onwards and so decreases the time available for these important metabolic processes. The alteration in the bowel wall permits the passage of toxins into the blood stream which also produce anaemia. Direct loss of blood may also occur from the ulcers, further increasing the anaemia.

CONGENITAL SYPHILIS: This condition is usually associated with a degree of anaemia. The factors producing the blood changes are, the general underdevelopment of such infants. They are weakly from birth, never able to suckle properly, and suffer from chronic catarrh of the nasal and alimentary tracts. All of these agents tend to interfere with digestion and allow the absorption of abnormal products. The spironema of the disease may have a direct effect on the red corpuscles. The alterations in the epiphyses characteristic of congenital syphilis may reduce the marrow spaces and divert the blood supply from/

from the haematopoietic tissue. There is usually considerable enlargement of the spleen.[34]

Hygienic conditions also contribute to the production of anaemia and will be discussed later.

NEPHRITIS. is an interesting cause of anaemia. In acute nephritis the anaemia rapidly becomes more marked as the disease progresses. The factors causing the anaemia are, the epistaxis and loss of red corpuscles in the urine, the retention of nitrogenous waste products interfering with normal blood formation, and the destructive influence of the toxin, which produces the changes in the kidney, on the red corpuscles.

In chronic parenchymatous nephritis the anaemia is always very marked.[35] In addition to the action of the toxin producing the disease, there is an alteration in the osmotic tension of the plasma. Where the parenchyma of the kidney is injured one of the chief results is an inability to excrete salt and water. The retention of these substances gives rise to the characteristic oedema. With the retention of water there is hydraemia and so a lowering of the osmotic pressure and a tendency for fluid to pass into the red corpuscles, leading to swelling and possibly rupture of any damaged or effete cells.

In chronic interstitial nephritis there is also a degree of anaemia. The retention of the products of metabolism/

metabolism which cause uraemia may be responsible for the anaemia. There is also loss of blood from haemorrhages.

Continuous loss of plasmic protein is given as a cause of anaemia.[36]

RHEUMATIC FEVER very frequently gives rise to anaemia of a severe degree. In a large proportion of cases of simple secondary anaemia a history of "growing pains", transient rashes and sore throats can be obtained. The exact cause of the anaemia is in doubt. High temperatures formerly may have been regarded as a cause but the introduction of salicylates in the treatment having removed this factor, there has been no corresponding diminution in the frequency of anaemia. A much more likely cause has been brought to light in the association with scarlet fever, tonsillitis and infective endocarditis, and the isolation of a streptococcus (sometimes haemolytic in character) from such cases. (Payne and Poynton.) This view is corroborated by the fact that the anaemia in rheumatic fever is always more severe when endocarditis is present, a lesion undoubtedly due to bacterial action.

CHEMICAL.

Lead poisoning is a very rare and remote cause of anaemia in children who are only exposed to it/

it when the metal or its salts are present to an unusual extent in water or foodstuffs. Lead poisoning may also arise from the child putting lead toys in its mouth or from lead paint used on cribs, toys etc. which the child sucks. Prolonged action of small amounts alone gives rise to anaemia; large amounts give rise to the effects of any irritant poison. The outstanding features of the blood changes in lead poisoning are the presence of punctate basophilia in the red corpuscles, some polychromasia and the presence of nucleated red cells.

PROTOZOAL.

Direct. Malaria which may occur in children who have lived abroad is the best example. The anaemia is due to the actual breaking down of the red corpuscles at the times of sporulation.

Indirect. Intestinal worms, e.g. thread worms and tape worms. In the former there is sometimes a severe degree of anaemia associated with an increase of the eosinophil leucocytes. The anaemia may be accounted for by the intestinal irritation which these parasites set up, leading to faulty digestion and assimilation. The actual amount of blood ingested by the parasite is small but it is conceivable that some toxin may be injected into the blood stream at the site/

site of attachment.[37] Infection by Borthiocephalatus latus is peculiar in that it gives rise to an anaemia indistinguishable from Pernicious Anaemia, and further that this only occurs when the parasite has died and is retained in the alimentary tract.

EXTHANTHEMATA. During the course of an ordinary case of scarlet fever the only alteration in the blood picture is a polymorphonuclear leucocytosis at the time of the appearance of the rash. In severe cases however anaemia may arise especially when there is ulceration of the throat and in cases with complications such as nephritis.

In these cases the complications are no doubt due to the causative streptococci and the anaemia is caused by the absorption of the toxins from the action of these organisms.

DIPHTHERIA. As in scarlet fever there is a polymorphonuclear leucocytosis in the early days of the illness. No definite anaemia has been noted in ordinary cases.

This disease presents an excellent example of extreme pallor due to action of the exotoxin on the heart in the later stages.

It might reasonably be expected that mild anaemia might arise from the action of the very potent exotoxin which has so powerful an action on the heart and the peripheral nerves.

NEOPLASTIC.

Intrinsic or neoplasms of the cells of the blood-forming organs.

The Leukaemias placed under this heading, may be considered as neoplasms of the haematopoietic tissues for, insofar as has been ascertained, there is no cause for the excessive leucocytic reaction. Further the leucocytes which are present in such enormous numbers in these diseases are often of very immature type, myeloblasts and lymphoblasts, such as never appear in response to ordinary infections or chemical stimuli.

When, in a case of leukaemia, pneumonia or other infection occurs, instead of a leucocytosis there is a remarkable fall in the number of white cells.[38]

Piney explains the blood picture by showing that in addition to the cells of the tumour foci, e.g. foci of small lymphocytes in lymphatic leukaemia, which have escaped into the blood stream, there are immature cells of other types thrown out by the hyperplastic haematopoietic tissue around these foci in the marrow.[39]

In the leukaemias the degree of youthfulness of the cells is greater than the degree of anaemia for the excessive growth of the white cells ruptures the walls of the sinuses in the marrow and allows the escape of immature cells into the blood stream.[40]

Acute/

Acute Lymphatic Leukaemia, the common form in childhood, arises quite suddenly. Usually the onset is marked by epistaxis or haemorrhage from the bowel. There is very marked increase in the percentage of lymphocytes, e.g., 96 per cent in a total white count of 100,000. Other well marked signs and symptoms are, enlargement of the spleen, of the liver, and the lymph glands, especially in the less acute cases, pallor and occasionally a purpuric eruption.
The degree of anaemia is severe, the number of red cells rapidly diminishes and may be as low as 600,000 towards the end.

The film shows marked anisocytosis and poikilocytosis with fairly frequent normoblasts, the white cells for the most part are lymphocytes, the proportion of large lymphocytes being greater in the more acute cases.

The disease is invariably fatal after six weeks to two months.

Chronic Lymphatic Leukaemia has similar signs and symptoms, only the enlargement of the lymph glands is much greater and in the blood film the predominating leucocyte is the small lymphocyte.

The total white count tends to be higher.

Myelogenous Leukaemia very seldom occurs in childhood. The disease is diagnosed by finding immature cells of the granular series in large numbers in the blood film/

film and by splenic enlargement. The anaemia is severe and normoblasts may number 20,000 per c.mm. Chloroma, in addition to changes in the leucocyte count similar to myeloblastic leukaemia there is a definite localised tumour of haematopoietic tissue characteristically situated around the orbit, and showing a greenish tint on section. The anaemia is marked.

In the leukaemias the anaemia is undoubtedly due to the enormous increase of white cells in the cavities of the bones encroaching on and diminishing the space available for the development of red cells. In the myeloid reticulo-endothelial system there is not the ability to perform one function to excess without at the same time interfering with the completeness of the other. It is improbable that this system will at the same time produce an excess of leucocytes and maintain the normal number of erythrocytes.[41]

Another factor in the production of anaemia is an ever increasing demand for red cells. The products of the bone marrow are abnormal and likely to have a shorter life, such corpuscles cannot maintain the nutrition of the marrow properly, further impairing its function and increasing the degree of anaemia.

The infiltration of the liver with the tumour-like masses of white cells may lead to interference with the/

the metabolism of iron and so to a reduction in the amount of haemoglobin available.

In acute lymphatic leukaemia a toxic factor may be present as is shown by the occurrence of a purpuric rash.

The following diseases are included in this group from their resemblance to neoplasms in many respects and since they involve the subsidiary seats of blood formation.

STATUS LYMPHATICUS. The pallor in this disease is very marked although the diminution in number of the red corpuscles is relatively slight, there being a much greater decrease in the percentage haemoglobin.

There is a demonstrable increase in the amount of lymphatic tissue throughout the body, during life seen in the tonsils and lymph glands, after death, in the thymus, spleen, tongue, and Peyer's patches. Other outstanding features are the Hassel's corpuscles in the spleen and the remarkable tendency to sudden death.

There is a leucocytosis of moderate degree affecting chiefly the lymphocytes.

The anaemia in this disease is part of the general underdevelopment which is shown in the thinness of the vessel walls, general muscular weakness and absence/

absence of secondary sexual characteristics if the child reaches adult years.[42]

HODGKIN'S DISEASE is also included under this heading since no cause has been found for the multiple swellings of the lymphatic glands.

Anaemia is never of very severe degree except in the terminal stages of the disease. The anaemia tends to be more marked during the rises of temperature (Pel-Ebstein syndrome) and waves of leucocytosis so characteristic of the disease. Again this is an example of the inability of the haematopoetic tissue to produce an excess of one type of cell and maintain the normal number of the others.

GAUCHER'S DISEASE, a peculiar condition involving the spleen. The disease is familial but not hereditary, and begins insidiously in infancy with pallor and progressive abdominal distension.
The spleen is markedly enlarged, firm and smooth, the liver is also enlarged. Brownish pigmentation of the skin may appear in patches and peculiar yellowish wedge-shaped thickenings of conjunctivae on each side of the cornea have been noted.

The lymph glands may be enlarged. The blood picture shows a diminution in red corpuscles with much greater diminution in the percentage of haemoglobin.
Leucopoenia/

Leucopoenia is characteristic although the differential count is normal.

Death occurs from intercurrent infection.

The causation of the anaemia has not been discovered. There is no crowding of the marrow spaces with white cells. The resemblance of Hodgkin's disease to tuberculosis seems to suggest a toxic cause. Piney suggests that the condition is neoplastic affecting the reticulo-endothelial system.

Gaucher's disease may have a somewhat similar explanation.

NEOPLASMS. Extrinsic, which includes any new growth other than the leukaemias, are very rare in childhood and very rarely give rise to the state of cachexia and anaemia so characteristic of advanced malignant disease in adults.

Sarcomata of the bones or of the kidney lead to anaemia for no very apparent reason, the actual amount of nutriment diverted to the growing cells of the tumour is small and so far as is known no toxic substance is liberated from a sarcoma. Ulceration and secondary infection of the tumour give rise to anaemia for the reasons detailed above.

When secondary metastases occur in the cavities of the bones the explanation of the anaemia is similar to that in the leukaemias. Anaemia of this type has been called myelophthisic.

METABOLIC.

Early. A child at birth has a quantity of iron in its tissues, chiefly the liver, in excess of the amount required for its immediate needs. The breaking down of large numbers of red corpuscles after birth increases this reserve of iron. The amount of iron containing pigment brought to the liver may be so great that the liver is unable to deal with it and icterus neonatorum develops. Increased viscosity of the bile delays its passage into the duodenum.

In a normal child the store of iron begins to be exhausted about the beginning of the sixth month and if the food ingested is deficient in iron anaemia develops, e.g., when a child is fed entirely on patent foods or over-diluted cow's milk (Bunge).

Anaemia from this cause arises in children of the poorer classes and is associated with laryngospasm and pylorospasm. Splenomegaly sometimes occurs, but this shows no definite relation to the degree of anaemia.[43] That other factors must be present is obvious from the fact that every child fed on milk alone up to the age of two years does not develop anaemia. Possible factors are, lack of vitamins, congenital or acquired disturbance of the blood forming organs and haemolysis resulting from prolonged

alimentary/

alimentary damage.[44]

That deficiency of iron is a factor is shown by the rapidity with which the condition improves when the diet is altered to include a sufficiency of iron or a simple tonic containing the metal or one of its salts.[45]

INFANTILE SCURVY, arising in circumstances somewhat similar to rickets which will be discussed below, first shows itself in children about six months old. The child is pale, thin and cries whenever its limbs are moved. Haemorrhages from the mucous membranes occur. The anaemia is only marked when there has been severe or repeated haemorrhages. Swelling of the gums and haemorrhage from them are only present when the teeth are through. Action of a toxic factor is shown by the appearance of a petechial rash in some cases.

RICKETS. This is perhaps the most frequent cause of anaemia between the ages of 1½ and 5 years, i.e., Group III apart from its association with Von Jaksch's anaemia.[46] The disease arises under conditions of improper nutrition, bad hygienic surroundings, lack of fresh air and sunlight.

The cause of rickets is an improperly balanced diet, under bad hygienic conditions. Excess of carbohydrate/

carbohydrate especially in the form of starch is an important contributory cause. Experiments in animals have shown that a deficiency or non-absorption of fat is a factor. Further investigation has shown that this is due to a lack of the accessory food factor, Vitamin D.

There is also deficient calcium metabolism.

The manifestations of rickets are changes in the bones, swelling of the epiphyses and various bowings, respiratory and alimentary catarrh, nervous phenomena, facial irritability, laryngismus stridulus, tetany, anaemia and enlargement of the liver and spleen.

Absolute deficiency of iron in the diet enters into the causation of the anaemia but the chief factor is probably an inability to utilise the available supply.

The part played by enzymes and catalytic agents in physiology and chemistry are well recognised but not understood.

Imperfect metabolism may be part of the general metabolic upset due to lack of vitamin D. which has recently been recognised as occurring with vitamin A in animal fats and oils and which may possibly have a catalytic action.

Related to the deficiency in vitamins is the lack of sunshine which will be discussed under Hygiene.

Another/

Another possible factor in the causation of the anaemia is the diversion of the blood supply from the marrow to the epiphyses.

The infections which so commonly accompany rickets also play a part in the causation of the anaemia.

The blood picture is not characteristic, decrease in red count and in the haemoglobin percentage, slight irregularity in size with occasional normoblasts in the more severe cases.

The alterations in the white cells are very variable and depend on the extent of the concomitant infection.

Later. Chronic Intestinal Indigestion is a suitable term to apply to cases with loss of appetite, loss of flesh, flatulence, constipation intermitting with diarrhoea and anaemia. Intestinal fermentation is set up in the presence of excess of carbohydrates. Cases which result more often from overfeeding and feeding between meals, than from underfeeding. Badly balanced diets also play a part in the causation of such symptoms.

The anaemia is due to the two factors found in many of the conditions already discussed, namely defective assimilation and the absorption of a toxin produced in this abnormal digestive process. The presence/

presence of a toxic factor is shown by the occurrence of punctate basophilia in some severe cases.

Endocrine Deficiencies.

Hypopituitarism, causing abnormal deposition of fat with associated faulty metabolism, is accompanied by a degree of anaemia.

Hypothyreoidism. Cretins usually show a degree of anaemia which since it is cured as the child responds to treatment with thyreoid extract, may be presumed to be due to the deficiency of the secretion of the thyreoid gland. The influence of this gland is very widespread during the period of active growth. The general slowing down of metabolic processes in cretinism will reduce the demand for new red corpuscles and the amount of oxygen necessary in the blood, so the amount of haemoglobin required is less than usual. The anaemia in these cases is not so marked as would be expected from the pallor and yellow tint of the skin, for there is marked thickening of the superficial layers of the skin with corresponding increase in opacity.

HYGIENIC.

The effects of bad hygienic conditions are very well shown in the slum areas of the larger cities, where the populace are literally buried in their narrow homes/

homes under a pall of smoke and fog scarcely ever penetrated by the health giving rays of the sun. The puny children, mentally very active from force of circumstances and struggle for life, are very frequently sufferers from anaemia in association with malnutrition, rickets and tuberculosis.

The principle factor in these cases is the absolute lack of sunshine whose effect in restoring or producing the healthy colour of the cheeks and vigour of body to the puny child of the slums, has been known for a long time. The sun is the ultimate source of all the energy in the world and, as through the agency of chlorophyll in the plant it builds up starch from simpler substances, so perhaps in the human body, through the agency of the haemoglobin or some other agent it may build up the very complex proteins of the living cells from simpler substances. Chlorophyll and haemoglobin resemble one another in that they require iron for their formation.

Recent work has tended to make clearer the relationship between lack of sunshine and defective diet. In vitro the exposure of certain substances of a fatty nature, e.g., cholesterol, to ultra violet radiation, brings about a remarkable change in their dietetic properties.

Animals/

Animals fed on a diet without fat but containing chemically pure cholesterol develop rickets, while the addition of irradiated cholesterol or ergosterol cures the rickets or prevents its occurrence.

It has been suggested that the ultra violet rays from the sun activate the cholesterol and other fatty constituents of the skin, producing vitamin D which is essential for the normal calcification of the bones and prevents the occurrence of rickets.[47]

Defective ventilation is an indirect cause of anaemia by contributing to a lowering of the child's resistance to infections which follows from living in over-heated, stuffy rooms.

The clothing of the majority of children of the poorer classes is unsatisfactory in that it is usually too plentiful and of the wrong texture. Heavy stuff garments are common, confining the perspiration and leading to defective functioning of the skin and lowering of the child's resistance to infection.

SUMMARY.

The mode of action of the various causes of secondary anaemia may be summarised.

1. Direct loss of blood.
2. Toxic action on the bone marrow causing interference with the formation of new cells.
3. Toxic action on the formed cells, causing lysis.

4./

4. Defective assimilation, lowering the amount of haemoglobin.
5. Toxic action interfering with the formation of haemoglobin.
6. Destruction of formed cells by parasites.

SECTION VI.

TREATMENT.

The treatment of any disease consists in the application of two great principles:-

I. Removal of the cause.

II. When that is impossible, removal or diminution of as many obstacles to recovery as are accessible.

The discussion of this subject may conveniently be divided into seven parts.

A. REMOVAL OF CAUSE.

Under this heading the methods applied more directly to the removal of the cause in secondary anaemias will be discussed.

Dealing first with the Physical causes, by the cessation of the haemorrhage from a wound the cause automatically removes itself and nothing further need be done.

In Haemophilia and Purpura Haemorrhagica on the other hand, although the particular haemorrhage which brings the child to the doctor has been successfully arrested (e.g., by the local application of adrenalin) some attempt must be made to prevent further haemorrhages. Children who are "bleeders" must lead a sheltered life to reduce the liability to accidents and so to haemorrhage.

Based/

Based on the theory that the delayed coagulability of the blood is due to a deficiency in calcium, salts of that metal have been given with varied success. Calcium is still prescribed in these cases as the lactate grs. 10 t.i.d. by the mouth. Recent work has shown that the blood calcium is normal in haemophilia and that the amount of calcium absorbed from the bowel is very minute.[48]

Intramuscular injection of the chloride is equally unreliable while being extremely painful, 5 to 10 ccs. of a 15 per cent solution being injected into the buttock every other day for a fortnight.

Combinations of calcium lactate and magnesium carbonate have been used.

Addition of the defective thromboplastic elements is possible by the administration of various sera. That the desired elements may not be altered by interaction with other tissue juices, the method of election is the intravenous route. The serum may be almost any freshly prepared sample. Antidiphtheritic serum is always available, also normal horse serum.

If it is intended to administer human serum, proper precautions must be taken with regard to the blood groups of the individuals.

A proprietary serum "Haemoplastin" has given good results in this disease as well as in haemorrhage from other causes.

The/

The dose is about 5 to 10 ccs. and should be repeated in 7 to 10 days to avoid the risk of anaphylaxis.

Normal horse serum by the mouth has had a beneficial effect on haemorrhage from the stomach etc., but nothing definite has been claimed for its use in haemophilia.

"Peptone Shock" has been used, from its action on the blood forming tissues producing a leucocytosis and possibly an accompanying increase in the thromboplastic elements.

The injection of whole blood (human) has been recommended.[49]

Subcutaneous and intramuscular routes are unsuitable, for a haematoma always forms at the site of injection.

In Purpura Haemorrhagica, methods similar to the above have been used. Since the defect is a diminution in number of the blood platelets and the above methods only modify the fluid and mineral contents of the blood, very little benefit is likely to ensue from their exhibition in this disease.

The influence of gravity in producing the purpuric rash must be minimised by putting the patient to bed and maintaining the recumbent position for at least 14 days after the disappearance of the rash.

Three therapeutic measures likely to be of

value are:-

(a) Splenectomy.

(b) Blood transfusion.

(c) Administration of arsenic.

(a) Splenectomy removes the chief organ of platelet destruction and allows these cells to accumulate in the blood stream.

This operation has been followed by a marked improvement in many cases with increase in the number of platelets. Unfortunately the operation is inseperable from a considerable risk and the rise in the platelet count is only temporary.

(b) Blood transfusion from a suitable donor supplies a number of platelets. Following transfusion the number may rise even to 300,000 per cmm. but it falls again in a few days as these are destroyed, never quite so low as before for the transfused blood seems to stimulate the normal formation.[50]

(c) Liquor arsenicalis, from its haemo-stimulant action, has given good results.[51]

Toxic, bacterial and chemical factors giving rise to anaemia are dealt with in a great variety of ways, the removal of the septic focus surgically, the treatment by specific antidotes, etc. which will not be discussed. After such methods have dealt with the cause/

cause there remains the alteration in the blood which still requires treatment. Sub-sections B. and C. deal with such cases.

The treatment of the Protozoal causes may be summarised by saying that the destruction of the protozoan causing injury to the patient is the aim, e.g. quinine in malaria.

The removal of the Neoplastic causes of secondary anaemia requires further discussion, for here attempts are made to influence the haematopoietic tissue directly.

In the Leukaemias and Chloroma various methods have been adopted to reduce the number of the white cells and to slow the rate of their production.

Drugs which fulfil this purpose are few in number.

Benzol m V in capsules t.i.d. is perhaps the best known.

Napthelene tetrachloride grs IV t.i.d. has been used.

The most successful method of bringing about any alleviation of the symptoms and a reduction in the number of white cells is undoubtedly the exposure to X-rays. Systematic exposure of areas including the spleen and long bones for 10 minutes is given every other day. The number of areas is such that each falls due for exposure once in 14 days.

The results are quite satisfactory in so far as the/

the splenomegaly is concerned, often a remission sets in, but no case of cure has been recorded.

Application of Radium over the spleen has similar results. The spleen goes down more slowly but in a recurrence never reaches quite the same size on account of the fibrosis which sets in.

These two mechanical methods seem to exert an inhibitory and destructive action on the cells in the bone marrow. Increased destruction of white cells is shown by the fall in numbers and by an increased output of uric acid in the urine.[52]

Splenectomy cannot be expected to have any beneficial result.

In Status Lymphaticus, Hodgkin's disease and Gaucher's disease all the methods used in the treatment of the leukaemias have been tried. No definite results have ensued, cases of Gaucher's disease have been benefited by splenectomy.

The removal of the Metabolic causes of anaemia can very frequently be accomplished.
In Early cases of improper feeding, a judicious change in the diet and attention to the amount of iron it contains, usually proves satisfactory, for the condition is of short duration.

The amount of iron required has been estimated for the various ages:-

Up/

Up to 6 months .5 mgs. per day.

6 to 12 months 1.5 " " "

In the 2nd year 2 " " "

The iron content of the commoner foods has also been estimated:-

Milk 1 pint contains	.08 mgs.	
Beef juice 1 oz. "	0.2	
Yolk of 1 egg "	1.4	
Oatmeal 3 tablespoons	3	53
Pruce juice 1 "	7	
Green vegetables 1 do.	3	

From these figures it is evident that iron is most easily given as yolk of egg or prune juice.

Rickets. In view of the known facts in aetiology, the treatment consists in supplying the deficient vitamins, usually in the form of cod liver oil combined with malt extract, in obtaining for the child the maximum amount of fresh air and sunshine possible.

In the larger town clinics have been set up for the treatment of rickets by artificial sunlight. This will be discussed later.

Infantile scurvy. Since this disease is due to deficiency of vitamin C, addition of this factor to the diet in the form of fresh fruit juice, e.g., lemon, orange, grape or scraped turnip, 1 dram daily, rapidly clears up the condition.

The anaemia improves rapidly when the tendency

to/

to haemorrhage is dealt with.

The treatment of Chronic Intestinal Indigestion in a child of 4 or 5 years of age is very difficult and disappointing. The prolonged action of the improper diet seems to exhaust the tissues of the alimentary tract so that the removal of the offending constituent from the diet does not lead to rapid improvement. A careful and judicious regulation and restriction of the diet may initiate recovery, the only drugs which may be used are simple tonics and these only with caution. Iron may be used when recovery has very definitely commenced.

The removal of the Endocrine deficiency is easy in hypothyreoidism, ¼ to ½ grain of the extract daily effects a considerable improvement. In the case of hypopituitarism and other endocrine deficiencies the appropriate extracts do not give similar results but the administration of thyroid extract often effects an improvement from the close inter-relationship of the endocrine glands.

Hygienic causes are perhaps the most trying to remove. Many of the mothers are ignorant, careless and untidy, allow their children to stay indoors, often in bed for the greater part of the day, only letting them out in the evenings when their elder brothers/

brothers and sisters have come home from school and are free to watch over them.

The children miss the benefit of the greater part of the somewhat scanty sunshine of our climate.

Only measures of the Public Health Authorities, by providing better houses and more open spaces, and education, can hope to eradicate the ill-health and anaemia arising from this cause.

One way of helping these mothers is to give them definite instructions about the feeding of their children. Little harm would result from the doctor using a standard diet for the various ages only to be modified when the child fails to gain weight. Too often the instructions given are vague. Let the doctor write down his instructions in terms of table spoons of milk and water, with the interval between feeds.

Another item which may be improved is the clothing of these children especially in the poorer localities. When a child appears to be at all out of sorts the first thing the mother does is to pile on several more layers of thick stuff garments, usually smelly and not too clean. A common feature of the many garments is their impermeability. The infrequency with which the clothing is removed to allow of a general bath is apparent when the child is brought to the doctor. The mothers and the children themselves, if they are old enough, show a remarkable lack of acquaintance with the/

the methods of undoing the various layers. Some simple instructions should be given. All clothes should hang from the shoulder and should have no constricting bands around the waist. A garment of wool, if the mother cannot be persuaded otherwise, may be allowed next the skin, a cotton shirt or chemise and not more than two thicknesses of tweed or woollen garments over this. The legs may be left bare provided the feet are protected by good socks and watertight boots.

Great benefit often results in these debilitated children of the poorer classes if the mother can be impressed with the importance of taking her children for a daily walk in the nearest park.

B. GENERAL LINES.

Environment. The advantages of fresh air and sunlight cannot be over-estimated. The insistence on a proper ventilation of the patient's apartment and a minimum of bed clothes consistent with the season, is amply justified. If the apartment is so fortunately situated as to have a southerly aspect, the patient's bed should be placed in or near the window to allow the sunlight to fall on the skin directly. The effects of sunlight will be further discussed under Artificial Sunlight.

Rest./

Rest. Diminution in haemoglobin content and in the oxygen carrying capacity of the blood lead to acceleration of heart rate and an increase in the amount of work the heart has to do. This increase in work coupled with the defective oxygen supply to the heart muscle itself leads to cardiac weakness and dilatation.

In infants very little can be done to lessen the work of the heart. The baby should not be lifted out of its cot except for feeding and bathing.

In older children, suffering from even the mildest degree of anaemia, an initial period of rest in bed should be insisted upon, at least a week, better a fortnight. Everything should be done to ensure the comfort of the child, no irksome regulations need be enforced if congenial amusements or tasks are provided.

Diet. The stomach and intestines share in the general atony and muscular weakness in cases of anaemia, with a tendency to dyspepsia and constipation.

In children under 3 yrs. the diet at first should consist of cow's milk and water only. The diet should be of the appropriate bulk for the child's age, i.e., up to 2½ mths. 3 ozs three hourly, later a number of ounces corresponding to the age in months up to 6 or 7 four hourly. The diet should contain a sufficiency of/

of calories for the heat requirements. This varies from 300 calories per diem in infancy to 1000 at the end of the first year.

During the first two days of treatment the diet of milk and water will not yield sufficient calories but the addition of 1 oz. sugar on the 3rd day increases the yield almost to the required level.

Two useful constants in feeding of infants are:-

1 oz. of milk yields 20 calories.

1 oz. sugar " 120 "

Cream is apt to increase any dyspepsia which may be present.

Diet is also discussed under the removal of metabolic causes on page 77.

If in children over 3 yrs. there is any tendency to dyspepsia great care must be exercised. Only bland non-irritating foods should be given and then only in small quantities, at frequent, regularly-spaced intervals. Such a diet would consist of milk, milk puddings, one egg, small portions of butter, sugar and cream. Drugs, especially iron salts, are better omitted at this stage and a simple bitter tonic given instead. Constipation should be dealt with using the milder aperients and salines.

With the improvement of the dyspepsia, or at the outset in cases which have none, the diet should still be small in bulk and given at regular intervals, for the/

the abdominal viscera as a whole and the stomach in particular, show a lack of tonicity and a deficiency of peristaltic movements which render digestion and assimilation imperfect and incomplete while at the same time leading to the retention of the residue and the production of toxins.

A diet at this stage would include milk, eggs, butter, fish, small portions of beef, mutton or chicken, preferably underdone and minced, cereals, of which the best is oatmeal, fruits raw and stewed, and green vegetables.

The child should be impressed with the importance of proper mastication which can be easily accomplished by making the child count the number of bites for each mouthful (Gladstone advocated thirty-two).

For the doctor's part, the teeth should always be examined and faulty ones dealt with. Often a child towards the age of six has very few efficient teeth left, in such cases minced foods should be ordered.

As the patient improves the diet should become more varied and liberal and gradually increased to an ordinary mixed diet.

Drugs may be introduced as the dyspepsia improves.

The following are better omitted altogether, tea, excess of sugar, condiments, pastry and excess of starchy foods.

Exercise./

Exercise.- After the initial period of rest the patient should be allowed to take a gradually increasing amount of exercise daily for it stimulates the muscular functions generally and aids digestion.

C. DRUGS.

Throughout the discussions on the removal of the various causes of secondary anaemia the writer has purposely avoided mention of the administration of arsenic and iron. These two drugs may be said to have a direct haemostimulant action, they are universally prescribed in cases of secondary anaemia after complete or partial removal of the cause, in cases of primary anaemia and in congenital anaemia.

The routes by which these drugs may be introduced into the body are three in number, orally, intramuscularly and intravenously.

ARSENIC.

Given by the mouth in small doses e.g., liquor arsenicalis m.II. t.i.d., the drug is absorbed almost completely in the stomach and duodenum, passes by the portal system to the liver whence it is distributed very widely throughout the body. After administration for some weeks arsenic can be recovered from all the tissues of the body even the hair. It is excreted in part by the urine but the bulk of the drug is retained in the liver, bones, hair etc. Patients develop a tolerance/

tolerance for the drug so it is customary to increase the dose e.g., rising by m. I. every other day until some effect is produced (e.g., conjunctivitis.). This tolerance has been explained by changes in the epithelium of the stomach which becomes more resistant to the drug.

The effects of arsenic on the blood-forming organs is to increase the output of red corpuscles. It may at the same time render them more resistant to the destructive action of the spleen. The nature of this stimulation is not known but on the analogy of increase in gastric secretion, it may be a direct action on the cells of the bone marrow probably from dilatation of the capillaries.

Preparations and Doses:-

Liquor arsenicalis (Fowler's Solution) alkaline in reaction m.I. upwards.

Liquor arsenici hydrochloridi, acid in reaction. m.I. upwards.

Sodium cacodylate ccs. $\frac{1}{2}$ to 2.

Organic preparations are widely used in general medicine and have been tried from time to time in the treatment of anaemia. Only preparations which liberate the AsO_3H_3 ions e.g., salvarsan give the action of the blood-forming organs.

Uses:- /

Uses:-

Arsenic is indicated in any case of anaemia where the number of red corpuscles is markedly decreased with relatively smaller decrease in the percentage haemoglobin, i.e., in cases with a relatively high colour index.

It has been used in all forms of anaemia but only gives satisfactory results with cases of the above type, e.g., pernicious anaemia.

In the leukaemias and Hodgkin's disease some temporary benefit has followed its administration.

The organic preparations have been given by injection in all varieties of anaemia. Success followed in pernicious anaemia alone, with a slight improvement in Hodgkin's disease and the leukaemias.

IRON.

From the knowledge that the most important constituent of haemoglobin is iron, administration of this drug is indicated in any case where the percentage haemoglobin is lowered.

When a simple inorganic preparation of iron is given by the mouth, e.g., m.V. of ferri citras, there is a slight local reaction on the epithelium of the stomach due to the action of the acid ions. The iron is absorbed from the duodenum and upper part of the jejunum, passes by way of the blood stream, probably as/

as minute particles in the leucocytes to the spleen and liver where it is stored.

Much of the drug given by the mouth is not absorbed and passes in the stools.

The absorbed iron may be utilised in the elaboration of haemoglobin or passes again into the blood stream and is excreted from the large bowel.

The course of iron during its absorption has been studied by microchemical methods.[54]

The action of iron is not clearly defined. That it acts by stimulating the blood-forming organs directly, has been disproved.

Zahn found that the recovery in rabbits rendered anaemic by haemorrhage and fed on a mixed, iron rich diet, was not accelerated as would be expected.[55]

It may increase the amount of available haemoglobin or it may provide an abundance of raw material in cases where the more complex iron-containing constituents of the diet are not assimilated.

Any of the iron preparations, especially the perchlorides, may set up dyspepsia and tend to cause constipation.

Preparations:-

A few examples of the more commonly used preparations will be given.

Ferric hydroxide, aqueous solution 5 per cent. m.V. to X. Non-corrosive, non-constipating, no digestive/

digestive impairment.[47]

Ferri carbonatus saccharatus

grs. X.

Blaud's pill.

grs. V. contains ferri sulphatus and potasi carbonatus.

Ferrum redactum.

grs. I to II. Metallic iron in fine form.

Liquor ferri perchloridi.

m. V. Very astringent and constipating.

Syrups of Iron:-

Syrup ferri iodidi. drms. ½ to I.

Syrup ferri phosphatus with strychnine, quinine etc. drms. ½ to 1 - all very pleasant and easy to take.

Colloidal solutions. Nonirritating.

Organic preparations are those in which the iron ion is combined with a protein molecule.

Haemoglobin itself is the first of these, either dried or as fresh bone marrow. Dose 5 to 15 grs. Also as a constituent of Virol where it is mixed with malt.

Ferrophytin, Ferratin, and Albuminate of iron.

The first, a combination of colloidal iron and vegetable phosphates, is stated to be nonirritating and nonconstipating.[56]

These preparations are expensive and are in no way advantageous. The complex molecules are of necessity broken down before the iron can be absorbed.[57]

Preparations/

Preparations for Injection:-

Two only need be mentioned.

Colloidal iron and manganese

m. V. intramuscularly every other day for 6 days.

Colloidal iron and arsenic and strychnine as in (Fuller)

R.	Sod cacodylate	mgs	30
	Strychnin sulph.	mg	1
	Colloidal iron	cmg	1
	Saline ad	ccs	5

5 ccs. given subcutaneously into alternate arms, daily for 5 to 6 weeks.

Uses of iron.

Administration of iron is indicated in any case where the percentage haemoglobin is lowered to a greater degree than the red cell count, i.e., cases with a low colour index. Its use is also indicated in cases where the signs and symptoms suggest that the food iron is not being assimilated properly. Chlorosis is the disease in which iron gives the best results.

Other drugs used in the treatment of anaemia are calcium salts, already discussed in the treatment of haemophilia, manganese and mercury. All these are of very doubtful value.

D. PRIMARY ANAEMIAS.

Von Jaksch's Anaemia. The efficacy of any treatment by drugs in this disease is very questionable, partly/

partly on the grounds that an endless variety of remedies have been claimed to give good results and that the tendency is for the majority of cases to recover if nothing but dietetic and hygienic measures are adopted.

Arsenic is perhaps the only drug which has any effect.

Mercury has been used and may be expected to give good results where the disease is associated with syphilis.

Pernicious Anaemia. Responds most favourably to administration of arsenic in increasing doses. Dilute hydrochloric acid after meals is beneficial.

Transfusion often starts a remission.

Recently treatment by liver extracts and a diet containing large quantities of liver have given good results.

Anaemia Gravis. Since this is essentially a cessation of the blood formation it is very resistant to treatment.

Arsenic and blood transfusion may stimulate the exhausted tissue but as a rule these cases do not respond to treatment.

E. ARTIFICIAL SUNLIGHT.

The physical investigations into the action of sunlight on the human body have shown that the changes are due almost entirely to the ultra-violet rays. The action of these rays has been studied chiefly in the higher regions of the Alps, for it has been found that such rays are for the most part absorbed by the impurities in the atmosphere at lower levels, especially in our cities.

The early work on natural helio-therapy was done by Rollier in the treatment of surgical tuberculosis. The children were gradually accustomed to the action of the sun by increasing very gradually the area of the body exposed and the time of exposure until they were out in the sun most of the day, with only a hat and waist cloth.

The effects noticed were, an erythema of mild degree, sometimes followed by desquamation, pigmentation in varying degrees and considerable improvement in general health.

In the attempt to make this benefit more widely available various sources of light were investigated. The ordinary carbon arc was found to give a moderate yield of ultra-violet rays. Subsequently the mercury vapour and tungsten arc lamps were invented. These have the advantage of giving out more ultra-violet

rays/

rays and much less heat.

Ultra-violet rays from any source falling on the skin are absorbed almost completely. They do not penetrate further than 1 millimetre. The action therefore is entirely confined to the skin and the blood circulating through it. The skin after exposure to the rays shows the erythema, desquamation and increasing brown pigmentation similar to those following exposure to natural sunlight.

The erythema is a vasomotor response.

The pigmentation is a protective response.

A further result of exposure to these rays is an alteration in the cholesterol so that it becomes activated. This activated cholesterol has the properties of vitamin D.

These results show the relationship between two widely separated methods of treatment in rickets which have both given excellent results.

The administration of cod liver oil supplies the vitamin D. in ready made form, while the exposure to ultra-violet rays brings about the elaboration of this substance from its inactive precursor already present in the body.

The rays also have an effect on the blood circulating in the vessels of the skin.

Exposure to ultra-violet rays increases the patient's resistance to infection.[58] The cellular and/

and haemoglobin contents are unaffected in normal children, but in rickets an increase in both is observed.[59]

Metabolism is increased.[60 & 61]

The technique and dosage are very complicated. The writer has experience of the mercury vapour lamp only.

Since it has been observed that very ill people shrink from bright sunlight and that moderate exposures to ultra-violet rays have had harmful effects in very debilitated children, the initial dose in all cases was very small. The arms, legs, and face were exposed at a distance of three feet for half a minute. The second exposure four days later was for the same length of time.

Table shows areas, and times of exposures:-

Exposure No.	Area	Distance	Time
1	Arms, face, legs	3 feet	½ min.
2	do.	"	1 "
3 & 4	do.	"	3 "
5 & 6	Whole body	"	Front 1 " Back 1 min.
7	do.	"	" 3 " " 3 "
8	do.	"	" 4 " " 4 "
9	do.	"	" 6 " " 6 "
10, 11 & 12	do.	"	" 8 " " 8 "

With these small doses no bad effects such as erythema were produced.

Indications/

Indications for use of ultra-violet rays.

From the action on the cholesterol of the skin the use of these rays is indicated in the treatment of rickets. Excellent results have been obtained.

The rays have been used in many other conditions of which anaemia and general debility in children is one, where although there is no marked deficiency in vitamin D some slight deficiency may exist and the increase following exposure to the rays may be the factor which brings about the beneficial result. The general increase in metabolism aids recovery.

Contra-indications.

Children with pyrexia from any cause or with a history and clinical appearances suggestive of active tuberculosis were not treated.

In addition to cases of rickets, general debility and anaemia, the writer used the method in a case of haemophilia (Case No.7)

F. ADDITIONAL METHODS.

Several methods of treating anaemia are still to be discussed.

Blood Transfusion. is by far the most important of these and is becoming much more widely used in the treatment of anaemia from all causes.

The immediate benefit which follows blood trans-

fusion/

transfusion after a severe haemorrhage is almost mechanical, a mere replacing of the lost blood. In addition to this result and in anaemia due to other causes the transfused blood seems to exercise a stimulating action on the blood forming organs of the recipient. It has been found in cases which were not improving under ordinary medicinal treatment that a small transfusion brought about a rise in the red cell count greater in extent than could be accounted for by the amount given and that this rise was progressive. This result suggests that in a case of anaemia the substance responsible for the normal production of red corpuscles, perhaps a hormone, is no longer present in an amount sufficient to produce its effect, a transfusion in such a case supplies an amount of this deficient substance. There is no clue to the nature of such a substance but its existance is highly probable.

The methods of carrying out blood transfusion belong rather to the province of the surgeon. In children the desired amount of blood can be obtained, using a paraffined syringe, drawing out the blood from the vein of the donor and at once injecting it into a vein of the recipient. More elaborate methods such as cutting down on the veins will not be described.

Suitable veins for the direct injection in a child/

child or infant are not always easy to find. Those in the cubital fossa are perhaps best and easiest, next, those about the ankle, and external jugular and as a last resort in infants, the injection may be made into the superior longitudinal sinus at the posterior angle of the anterior fontanelle. This procedure is not free from risk and requires a special short needle.

The blood given may be either whole blood which is obviously the better, or citrated blood which has the great advantage that it can be transported and that donor and recipient may be in different rooms. It is remarkable that citrated blood which does not coagulate "in vitro" is as efficient as whole blood in the arrest of haemorrhage. The amount of blood given must vary with each case, but a good working rule is 8 to 10 ccs. per pound body weight.

In treating a case of severe anaemia the transfusion should be repeated in from five to eight days until the blood examination shows that active regeneration is taking place.

Small transfusions given frequently are of greater value than an occasional large transfusion.[62]

Indications for Transfusion.

Blood transfusion is indicated in all cases of severe anaemia, also in the less severe cases where the cause is infective in nature, for the addition of fresh/

fresh antibodies in the transfused blood aids in combatting the infection and hastens recovery.
For the arrest of haemorrhage from any cause.

Results.

Excellent results have followed transfusion in a great variety of cases of anaemia. Considerable prominence is given to this method of treatment in the latest works of blood diseases in childhood.
Case No.10 shows a remarkable response to transfusion.

Administration of serum.

By the mouth, M.10 of horse serum taken from animals whose blood is in a state of regeneration after a recent haemorrhage, may be given twice daily.
(Fuller.)

By injection subcutaneously or intramuscularly of serum or what amounts to almost the same thing, an injection of whole blood may be given into the buttocks in doses of 10 ccs. Any foreign serum seems to have a stimulating effect on the bone marrow.
Intraperitoneal injection of human blood has been used.[63]

Cod liver oil.

This substance may be mentioned in a discussion of the treatment of anaemia for apart from its almost specific action in the cure of rickets, the administration of this substance has a beneficial effect in many cases/

cases of anaemia. Perhaps in addition to the gross deficiency of vitamins which gives rise to rickets, there may be milder degrees of "hypovitaminosis" which produce anaemia and the lesser degrees of general ill-health in childhood.

In cases of tuberculosis the additional nourishment supplied by the fat in the oil has a further beneficial action. The extra vitamin A supplied in the oil stimulates general metabolism and growth. Dose 15 to 30 minims twice daily as emulsion or mixed with fruit juice.

G. LIVER TREATMENT.

During feeding experiments to ascertain the effects of various diets on the rate of recovery from anaemia due to loss of blood it was found that a high protein diet accelerated the rate of recovery. (Whipple).

Minot and Murphy have carried out this principle in the treatment of pernicious anaemia, including in the diet large quantities of liver. Remarkable improvement was noted in cases taking 150 to 225 grams of fresh liver per diem. The results were not affected by cooking the liver. They also obtained good results from the exhibition of liver juice.

After three days treatment by this liver diet a prompt/

prompt increase in the number of reticulated red cells is noted up to 15 to 40 per cent. This increase is however only temporary, the percentage dropping to normal after about 16 days when an increase in the red cell count has become definite. The increase in the red cell count goes on steadily until it is almost normal.

In the majority of cases the red cell count can be maintained at about 4,000,000 by giving 180 grams of liver pulp flavoured with orange juice twice daily, mid-morning and afternoon.[64]

These authors are of the opinion that liver treatment may benefit other patients but that it is not effective in all forms of anaemia.

Recently potent fractions have been isolated from the liver and used in the form of extracts. The results from the use of such preparations compare favourably with those of the use of "whole" liver and they have the additional advantage of being more palatable and a much smaller dose.

The writer has used such an extract in the treatment of one case, No.10.

SECTION VII.

NOTES OF CASES.

In this section the writer gives short clinical notes of cases, with details of treatment, progress, blood examinations and results. A short discussion is given after each case.

Case No.1. E.H. Aet 11 yrs F.

The child was brought to hospital on account of severe nose bleeding. The family history was irrelevant. Previous history of measles, whooping cough, chicken pox and rickets in infancy. No previous epistaxis.

Sudden spontaneous epistaxis occurred on 3.3.28 while in bed, and continued for about 10 mins. Next morning there was further bleeding and again in the evening. Physical examination showed a well developed, well nourished girl with marked pallor of lips and facies. Cheeks slightly flushed, conjunctivae pale. She felt giddy when she tried to stand up. Pulse rapid 114, soft in character. No murmurs were heard over the heart. Nothing else abnormal was found.

Blood/

Blood Counts		R.B.Cs.	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	4.3.28	3,830,000	7,500	65	.85	54	32	8	1	-	3	2
2	5.3.28	3,420,000	7,640	60	.76	56	25.5	14	-	.5	2.5	1.5
3	6.3.28	3,905,000	8,440	55	.70	48	40	10	-	-	4	1
4	7.3.28	3,880,000	5,880	65	.84	41.5	34	17	.5	-	4	2.5
5	9.3.28	4,230,000	6,040	65	.77	44	37	11	-	-	4	4

Films.

1. Quite normal in appearance.

2. One nucleated red cell discovered with some polychromasic cells.

3. A few nucleated red cells, a number of microcytes and some polychromasia. One typical myelocyte (neutrophil) found.

4. No nucleated reds or myelocytes found. Still some microcytosis and polychromasia.

5. Polychromasia the only abnormal finding.

Diagnosis, Spontaneous epistaxis.

Treatment and Progress.

4.3.28. At rest in bed. Bleeding recurred at 7 a.m., nose packed with adrenalin soaked gauze.

5.3.28. No further bleeding, packing was removed.

She made an uneventful recovery.

Discussion.

A case of anaemia of moderate severity due to a physical cause, with typical blood findings.

The red cell count shows a fall after 24 hrs., a further slight fall next day and a fairly rapid rise during the next five days.

The/

The changes in the white cell count show that the leucocytosis following loss of blood takes place very soon after the haemorrhage and was already present at the end of 24 hrs. since subsequent counts were lower. Also the percentage of polymorphs fell after the second day.

Alterations in the characters of the red corpuscles in the films were never marked and were only present for a few days.

Results.

Recovery from a moderately severe anaemia without treatment.

Case No.2. I.M. Aet 5 mths.

The baby was brought to hospital because it had not been gaining weight, was constipated and fretful. The family history was very unsatisfactory, the mother was very dull mentally and had scarring at angles of the mouth and an opacity of the cornea suggesting syphilitic infection or inheritance. The first child was premature and only lived three days. The past history showed great negligence with regard to the times of feeding and also to the amounts given. The mother stated that after the first fortnight during which she was in hospital, the feeds consisted/

consisted of "half a teacupful of cow's milk with some water." This somewhat indefinite feed was given at about 3 hourly intervals. The baby weighed 7½ lbs at birth. Up to age of 2 mths. it had gained 1½ lbs; since then it had failed to gain although the feeds were increased to a full teacup of milk with porridge, bread, tea etc. There was some vomiting after feeds. The child became pale, weakly and thin. Stools became "putty-like".

On admission the child weighed 8½ lbs and was a typical marasmic infant, sucking its thumb, eagerly gulping down its feeds and always hungry.

The physical examination revealed nothing beyond the general undernutrition. There was pallor of the mucus membranes but no oedema. Stool "putty like, somewhat crumbly with fine white curds, "soap stool". No murmurs were heard over the heart. The liver and spleen were not enlarged.
The Wassermann reaction was negative.

Blood counts.

		R.B.Cs.	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M	My
1	21.3.28	3,990,000	10.640	75	.96	31	53	9	1	-	3	2	1
2	28.3.28	4,350,000	12,040	65	.75	22	46	26.5	2	-	1.5	1.5	-
3	4.4.28	5,280,000	10,200	75	.73	25	47	13.5	2.5	-	6	6	1
4	19.4.28	4,720,000	8,800	75	.79	34	37	18	2	-	5	4	-
5	24.5.28	4,860,000	9,460	75	.78	36	46	11	1	-	2	4	-

Films.

1. Slight anisocytosis, all the red cells well stained. The polymorphonuclear leucocytes showed a fair number of "band forms".

2. No abnormal features detected.

3. No abnormality in red cells. One myelocyte found.

4. No abnormality detected.

5. Normal film.

Diagnosis. Chronic indigestion from mismanagement.

Treatment and Progress.

Treatment consisted in a regulation of the diet, at first weak dilutions of cow's milk and water and sugar. The interval between feeds was 2 hrs. then 3 hrs., the amount increasing gradually as the child improved from 2 ozs. to 6 ozs. Virol I dram daily was given from 1.4.28.

The child did very well, leaving hospital at the end of 2 mths. weighing 11½ lbs., a gain of 3 lbs.

Discussion.

The anaemia in this case was only of moderate degree and of the alimentary type, from chronic intestinal indigestion.

The high colour index in count No.1 is difficult to account for, faulty reading of haemoglobinometer being the most apparent.

Result.

Marked improvement.

Case No.3. A.W. Male Aet 5 yrs.

In December 1927 the patient had a typical attack of measles with marked catarrh of the respiratory passages from the onset. On 20th Jan. he complained of severe pain in the left side which heralded the onset of a left sided broncho-pneumonia. The temperature did not settle and the dullness on the left side became absolute, suggesting an empyema. This was confirmed by thoracocentesis. The pus contained pneumococci. Aspiration on two occasions drained the pleura but when the pus accumulated for the third time it was decided to resect a portion of rib and drain the empyema.

Family history:- negative.

Previous history:- no other infectious illnesses, general health good.

Examination, just before operation showed a very pale little boy, with a hectic flush on the malar regions. Apart from the signs typical of empyema nothing abnormal was discovered. The heart was displaced to right but no haemic murmurs were found.

He withstood the operation very well and apart from two occasions when the drainage became occluded with consequent rise of temperature, he made an uneventful recovery.

Haemic/

Haemic murmurs were detected on 17th Feb. at the mitral and pulmonary areas.

On 18th March murmur confined to the pulmonary area, continued present until 16th April.

Blood counts.

		R.B.Cs	W.B.Cs	HB	CI	P	SL	LL	E	B	T	M
1	6.2.28	3,150,000	21,400	50	.78	78	11	8	1	-	1	1
2	18.2.28	2.810,000	15,760	40	.71	62	15	9	.5	-	2.5	1
3	3.3.28	3,570,000	20,300	65	.91	75	18	4	1	.5	1	.5
4	18.3.28	3,650,000	13,550	55	.76	53	26	11	1	1	4	4
5	1.4.28	4,480,000	12,920	70	.79	57	21	15	1.5	.5	2.5	2.5
6	16.4.28	4,510,000	10,800	75	83	48	37	8	2	-	2.5	2.5

Films.

1. Well marked anisocytosis and poikilocytosis present. Slight polychromasia and a few normoblasts were found.

2. Anisocytosis and polychromasia present but only very slight poikilocytosis.

3. Anisocytosis was the only abnormality found in the red cells, except some polychromasia.

   The "Schilling index" of the polymorph neutrophil leucocytes gave the following percentages.

Myelocytes	1 per cent	) Total
Meta myelocytes		) neutrophil
(Young and "band" forms)	11 " "	) leucocytes
Polymorphs	63 " "	) 63 per cent.

4. Anisocytosis and slight polychromasia present in a few of the red cells.

"Schilling Index"		) Total
Myelocytes	- per cent	) neutrophil
Meta myelocytes	6 " "	) leucocytes
Polymorphs	47 " "	) 53 per cent.

5. Red cells normal.

"Schilling/

"Schilling Index"			Total
Myelocytes	-	per cent	neutrophil
Meta myelocytes	5	" "	leucocytes
Polymorphs	52	" "	57 per cent.

6. No abnormal findings.

Diagnosis. Eypyema with secondary anaemia.

Treatment.

The treatment in this case consisted in the removal of the cause surgically. The patient was given a generous mixed diet and daily doses of Virol.

Discussion.

A case of anaemia due to absorption of toxin from a septic focus.

The blood findings are typical of the effects of any severe infection by pyogenic organisms, namely a high leucocytosis chiefly polymorphic, a degree of anaemia and a diminution in number of the eosinophil and basophil leucocytes. That the haemopoietic tissues responded satisfactorily was shown by the presence of signs of regeneration in the red cells and a shift to the left of the "Schilling Index".

The normal figures of this "Index" are:-

Myelocytes	-	
Metamyelocytes	4	
Polymorphs	63 per cent	65

Result.

Excellent recovery from a moderately severe degree of anaemia.

Case No.4. R.S. Male Aet 4 mths.

Complaint. Almost from birth the baby had difficulty in suckling. When feeding it was seized by fits of choking and gasping respiration.

The family history was negative.

Previous History.

The labour was difficult. The child was premature, very cyanosed after birth and continued so for several days. The feeding was unsatisfactory from birth, at first Nestlé's milk and water later with the addition of Virol. It was fed "whenever it was awake".
(Weight at 10 days was 5 lbs.)

Physical examination.

The child was very much under-developed, only weighing 6 lbs. and very pale.

During a paroxysm the respirations became noisy and laboured, the chest was expanded yet there was indrawing of the lower ribs on inspiration. The breath sounds were well heard, inspiration harsh and expiratory prolonged; no adventitious sounds were present. There was no evidence of congenital pyloric stenosis and the stomach tube passed normally.
The pulse was very feeble but no cardiac murmurs were detected.
X-ray of chest did not reveal any enlargement of the thymus.

The/

The child was quite unable to suckle after admission so was fed nasally. Two days later the temperature rose to 100.2 with dullness at the bases of the lungs. Next day the pulse became uncountable, temperature 102.6 and respirations very rapid. The child had developed a hypostatic pneumonia. Died same day.

At the post-mortem the general atrophy of the tissues was very noticable. On opening the thoracic cavity the lungs bulged forwards, with emphysematous "blebs" along the margins. Both bases were congested. No marked narrowing of the larynx or trachea was found. The liver was pale. There was no enlargement of the spleen. Sections showed fatty degeneration of the liver and atrophy of the cells of the centres of the lobules.

Section of the spleen showed signs of passive congestion.

Blood count.

	R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	R	T	M
9.2.28	2,795,000	9.950	40	.72	39	43	10	1	-	4	2

Film.

The red cells showed marked anisocytosis, slight poikilocytosis but no polychromasia. Four normoblasts were seen.

The white cells were largely lymphocytes. One myelocyte was seen.

Diagnosis.

Laryngospasm with wasting due to inability to suckle.

Discussion.

A case of anaemia of severe degree due to diminished intake of food. Signs of regeneration were almost completely absent showing that the blood forming organs were approaching a state of exhaustion. The absolute number of white cells was lowered hence the rapidly fatal result of the basal pneumonia.

Result. Death.

Case No.5. G.W. Male Aet 5 yrs.

During the two months prior to admission the patient had become listless, disinclined for play and was very "sleepy". His appetite was poor and pallor was noticed. He had a cough.

Family History.

Father and Mother both healthy. There were six children, the patient being the fourth. The eldest, a boy of 11 yrs., was then unable to attend school on account of anaemia, he was very pale, with cold extremities, feeble pulse. Haemic murmurs were present but no enlargement of the spleen and no alterations in the conjunctivae other than pallor. The second, a girl 8 yrs., was healthy. A boy, aet 7 yrs. was pale and had a haemic murmur at the pulmonary area. The two younger children, aet 3 yrs and 1 yr. were healthy.

Previous/

Previous History.

Since he was 18 mths. old the boy has never been healthy, at that time he had measles followed by whooping cough. The cough never cleared up properly. In Oct. 1927 he had bronchopneumonia which dragged on for two months. It was during this illness that enlargement of the spleen was noticed. He responded to treatment on general lines with the addition of Syr. ferri. phos. co. drms ½ t.i.d. On 12th Jan. 1928 the spleen was no longer palpable. Soon after his return home the cough became worse, he became pale, listless and weak.

Examination on 22.2.28.

The patient was a very apathetic, pale little boy, well nourished but underdeveloped. The spleen was palpable 2 finger breadths below the costal margin in the anterior axillary line. No haemic murmurs were detected. In the chest were the physical signs of bronchitis, with some impairment of resonance and a coarse pleuritic rub at the right base. The tonsils were enlarged but not markedly septic. The conjunctivae were not thickened at the inner canthus. A few small lymph glands were palpable in the neck.
No tubercle bacilli were found in the sputum and von Pirquet's reaction was negative. Blood "Wassermann" was negative.

Blood/

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	22.2.28	3,335,000	8.280	45	.67	35	47	11.5	2.5	.5	1.5	2
2	6.3.28	4,130,000	6,850	60	.73	32	46	17	1	1	4	1
3	21.3.28	4,410,000	9,800	65	.74	36	39	14.5	5	.5	2.5	2.
4	4.4.28	4,770,000	11,950	65	.71	46	26	16	3	-	4	5
5	11.4.28	4,690,000	12,210	70	.73	42	38	11	2	-	4	3
6	8.5.28	4,310,000	9,320	65	.75	35	43	11	7	2	1	1.

Films.

1. The red cells were very pale, no anisocytosis no poikilocytosis and no polychromasia.

2. Slight anisocytosis, a number of microcytes being present.

3. Two immature white cells of the granular type were found, Red cells normal.

4. One immature white cell was found. The red cells were pale but normal in size and shape.

5. Red cells normal.

6. Slight anisocytosis present.

Diagnosis.

Chronic bronchitis with secondary anaemia.

Treatment and Progress.

At first treatment was directed to the alleviation of the respiratory catarrh.

6.3.28. Liquor arsenicalis minims I t.i.d. was given The dose was increased at intervals of two days to M. IV t.i.d. Discontinued on 6.4.28.

Virol was given throughout in doses of 1 dram daily.

Tonsillectomy was performed on 4.4.28. The tonsils after/

after removal were soft and "pussy".

The patient's condition improved slowly, he began to be more alert and he was running about prior to his operation. The pallor was only slightly diminished. He withstood the operation well and was up again in three days.

8.5.28. Reported. Had been much brighter mentally and had taken his food well. He still had a cough. Physical signs of bronchitis were found on both sides of the chest. Colour was fairly normal. Pulse rate 96. No haemic murmurs were found. The spleen was just palpable on deep expiration.

Discussion.

A difficult case in which to make a diagnosis in view of the leucopoenia and the occurrence of anaemia and splenomegaly in another member of the family. Banti's disease seldom occurs in so young a patient and none of the accompanying signs of Gaucher's disease were present, e.g. phlyctenules, pigmentation, etc.

The anaemia was of secondary type from absorption of toxins.

Result. Considerable improvement.

Case No.6/

Case No.6. A.D. F. Aet. 3½ yrs.

Complaint ; swelling of abdomen and diarrhoea for 3 weeks.

The family history was poor, the mother was very pale, had been losing weight, and had a cough. No physical signs of phthisis found. Maternal uncle was then in a sanatorium with phthisis. A brother died aet 1½ yrs from abdominal tuberculosis and a sister aet 11 mths. from meningitis. Two other children were in good health. The home surroundings were poor but clean.

Previous history was almost negative. The patient had measles aet. 1 yr and suffered from occasional "colds in the head". She was breast fed for nearly two years.

The present illness began with the gradual onset of diarrhoea. The stools which had a very bad odour and a greenish colour, were passed six to eight times in the day. The child became listless, lost her appetite and became very pale.

Physical examination on 7.12.27 revealed a small under-nourished little girl whose luxuriant dark eyelashes and hair were, in marked contrast to the pallor of her complexion. When she stood up there was obvious abdominal swelling.

The abdomen measured 34 ins. in circumference at the level of the umbilicus. The umbilicus was not protruding. The swelling was symmetrical. On palpation/

palpation there was a general increase in resistance but no abnormal masses were detected. On percussion no evidences of free fluid or enlargement of the spleen or liver were found. The mouth was in an unhealthy condition, the teeth were dirty and carious, the tongue pale and furred, the tonsils slightly enlarged. In the chest apart from a "turning out" of the lower ribs due to the abdominal swelling, no changes of significance were found. The heart was normal and no haemic murmurs were heard. There were some small lymph glands palpable in both sides of the neck.

Diagnosis - Abdominal tuberculosis.

Blood counts.

	R.B.Cs.	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M.
7.12.27	4,190,000	12,150	55	.67	45	38	11	3.5	-	2	.5
10.1.28	4,320,000	9,840	60	69	38	48	11	1	-	2	1

Films.

7.12.27. Slight anisocytosis, poikilocytosis were present.

10.1.28. Still some irregularity in size and shape present.

No changes in the white cells noted.

Progress and treatment.

The diarrhoea responded to treatment on the usual lines.

On 28.12.27. she was free from diarrhoea and able to get up. Abdomen measured 34 ins. Syrupus ferri iodidi drams I was given twice daily.

10.1.28/

10.1.28. Child was much brighter and took her food well. No recurrence of the diarrhoea. Abdomen measured 31½ ins. Liver just palpable below the costal margin.

Discussion.

An anaemia of mild degree due to absorption of toxin from the foci of infection in the gastro-intestinal tract. Defective assimilation was a subsidiary factor.

Result. Slight improvement.

Case No.7. W.L. Male. Aet 6 yrs.

Complaint. Bruises on forehead and over shins. In view of the fact that the boy had had several severe bleedings previously the family history was investigated closely. One brother aet. 8 yrs, was healthy. Two maternal uncles and one maternal great-uncle were the only male relatives alive. None had shown any tendency to bleeding. The father was killed in an accident.

Previous History.

A full time baby, delivered naturally, there was no bleeding at the separation of the cord. The patient developed normally up to the age of 2 years when a severe bleeding followed a cut on the lip. Two years later there was severe bleeding from a cut finger.

No/

No rash of a purpuric nature was ever noticed.
He has not had measles or scarlet fever.

Present Illness.

In October 1927 complained of severe pain in left hip and knee. X-ray showed no evidence of tuberculous infection but he was treated as an early case and sent to the seaside on a splint. Two days after his return (Nov. 21st) he fell and cut his forehead. There was profuse epistaxis and considerable bleeding from the wound. Ordinary measures failed to arrest the haemorrhage so he was sent to hospital. The epistaxis ceased soon after admission but the oozing from the wound continued for about 6 hrs. Firm pressure and adrenalin pads were the effective remedies.

Reported on 2nd Mar. 1928 with the bruises noted above. No further bleedings had occurred.

Physical examination showed a well developed, well nourished boy, of fair complexion and somewhat pale. Detailed examination did not reveal any outstanding abnormalities. The pulse rate was 102. The lips and conjunctivae were pale. No haemic murmurs were heard. The spleen and lymph glands were not enlarged.

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	2.3.28	4,850,000	6,900	70	.72	47	37	8	2	1	3	2
2	27.3.28	4,640,000	8,680	75	.81	57	21	9	3	3	4	3
3	23.4.28	4,600,000	10600	70	.76	60	19	8	3	-	4	6

Films/

Films.

1. Apart from a slight irregularity in size and a slight achromia of the red cells, the films were normal. One myelocyte was found.

2. Again a palely staining film, otherwise normal.

3. No abnormalities of the red or white cells were found.

Coagulation time of a drop of blood on a slide was noted. The drop used for this test was taken after the other tests.

1. 23 mins.
2. 15 mins.
3. 12 mins.

After taking the drop for the above test the succeeding drops were dried off with a piece of filter paper.

Bleeding time.

1. 4 mins.
2. 4 mins (A second prick had to be made, the first having stopped bleeding after filling the pipettes.)
3. 5 mins.

Diagnosis.

The writer feels justified in diagnosing the condition as haemophilia, although there was no history of bleeding in the family.

Progress and treatment.

The boy was kept in bed for a few days then a course of artificial sunlight was given.

27.3.28. Reported after 6 exposures. Mother thinks his general health has improved, takes his food well. His mother has great difficulty in preventing him from taking/

taking part in games with other boys.

27.3.28. Completed the course of 12 exposures to ultra-violet rays.

General health fair. No recurrence of haemorrhages.

Discussion.

An interesting case which may become more definitely Haemophilic in nature as time goes on. The writer used the artificial sunlight for two reasons. It has a beneficial effect on general health and may conceivably have some action on the coagulability of the blood. From the first six exposures no striking changes in the blood were produced.

The difference in length of coagulation time before and after the course of ultra-violet radiations was too small to justify a conclusion that such radiations affect the coagulation time.

No appreciable degree of anaemia could be said to exist in spite of the definite pallor.

Result.

Blood condition unaltered, some improvement in general health.

Case No.8/

Case No.8. A.T. Male Aet 2 yrs.

Complaint of cough, loss of appetite, feverishness at nights and pains in the left knee for four days.

The family history and the previous history revealed nothing of interest.

At time of examination the little boy was obviously ill, he was very pale and thin, and breathing quickly and somewhat noisily. In his chest numerous physical signs of bronchitis were found, but no definite consolidation. The pulse was very rapid, 140 and feeble. The heart was not dilated or displaced. No murmurs were heard. There was no enlargement of the liver or spleen. Locally there was slight swelling of the left knee with redness, child cried out when the limb was moved. Three days after admission a fullness was noted over the front of the left hip. The temperature was intermittent. X-ray examination showed advanced arthritis with erosion of the head of the femur and acetabulum. Next day a quantity of pus was passed per rectum. 9.1.28 multiple incisions made over the joint. The child was extremely ill and very little hope was entertained for his recovery. Continued in this precarious condition for 3 weeks, when an accumulation of pus developed in the ham-string muscles, incised and drained.

First blood count done on 9.2.28. when the temperature had settled and the amount of discharge had lessened.

Blood counts.

	R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1 9.2.28	2,830,000	35,250	40	.69	78	15	6	-	-	-	1
2 28.2.28	3,150,000	23,350	40	.64	77	16	5	-	-	1	1
3 11.3.28	3,695,000	39,950	50	.69	79	13	5.5	-	-	1.5	1
4 25.3.28	3,720,000	19,240	50	.67	67	14	10	1	1	3	4
5 8.4.28	4,370,000	15,240	60	.72	52	33	8	-	1	2.5	3.5
6 22.4.28	4,620,000	15,750	70	.76	37	48	9	2	.5	1.5	2
7 5.5.28	4,760,000	16,520	70	.74	38	46	8.5	3.5	.5	2	1.5

Films.

1. Anisocytosis and poikilocytosis present. No polychromasia. Two normoblasts found.

2. Anisocytosis and poikilocytosis present. 7 Normoblasts found.

3. Anisocytosis but no poikilocytosis present. A few polychromatic cells found.

4. Anisocytosis with a number of macrocytes present.

5. Slight anisocytosis present.

6. No abnormalities of red cells detected.

7. Films were normal in all respects.

"Schilling Index".

Film No.	2	3	4	5
Myelocytes	2	1	-	-
Meta myelocytes	9	12	7	3
Polymorphs	60	66	55	39
Total neutrophil leucocytes	71	79	62	42

Diagnosis.

A case of severe secondary anaemia following septic arthritis of the hip joint.

Treatment and Progress.

12.2.28 Three days after the first blood count there was a sharp rise of temperature to 104.2°.

Next/

Next morning there was a copious discharge from the left ear.

21.2.28. Developed typical measles rash with slight temperature.

3.3.28. Discharge from the wounds very slight, none per rectum.

Given as much food as he would take and Virol drams I t.i.d.

17.3.28. Wounds healed, temperature normal and general condition very much improved.

From this time improved steadily, gained weight rapidly and left hospital on 5.5.28 a healthy boy except for the ankylosis of the hip joint.

No haemic murmurs were heard at any time in this case.

Discussion.

The case is of interest as showing the remarkable powers of recovery of the child from the effects of prolonged suppuration and drainage. The blood findings were typical and showed a "post-infective lymphocytosis" also absence of eosinophil and basophil polymorphs during the period of high leucocytosis.

Result.

Recovery following surgical removal of the cause.

Case No.9/

Case No.9. W.W. Female Aet 11 yrs.

Complaint was a feeling of weight in stomach, general weakness and pallor for several months. The family history was negative.

Previous illnesses were chickenpox, aet 1 yr., measles followed by bronchitis, aet 1½ yrs, whooping-cough aet 3 yrs.

Present illness began very insidiously about four or five months ago. The patient had been growing rapidly so her mother did not seek medical advice until it was apparent that something more than mere rapidity of growth might be affecting her health. The pallor was noted some time after the pain and indigestion had manifested themselves. Bowels were constipated, there had never been any vomiting.

Physical examination showed a tall overgrown girl with pale complexion. The mucous membranes were pale.
The pulse rate was 104 and the wave small.
The heart was enlarged to the left ¾ ins. beyond the nipple line in the 5th intercostal space. A soft, blowing, systolic murmur was heard at the mitral area but not at the pulmonary. In the abdomen nothing abnormal was found, the spleen was not enlarged, there was no tenderness in the epigastrium. Urine was free from albumen and pus. No physical signs of pulmonary disease were detected.

Blood/

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	4.3.28	4,380,000	9,200	75	.87	78	15	35	1	-	1.5	1
2	14.3.28	4,620,000	9,750	65	.71	58	30	6.5	1.5	.5	3	.
3	29.3.28	4,560,000	8,040	70	.77	52	31.5	9	3	.5	2.5	1
4	4.5.28	4,490,000	8,160	70	.78	49	31	11	2.5	.5	3	3

Films.

1. Slight irregularity in size of red cells present.

2 & 3 Nothing abnormal detected.

4. No abnormalities of red or white cells found.

Treatment and progress.

The epigastric pain cleared up in a remarkable manner when the constipation was relieved by an aperient and an enema. The diet was restricted for one week, afterwards an ordinary mixed diet was allowed. Blauds pill grs V was given from 14.3.28 thrice daily. Reported 4.5.28 with further epigastric pain for two days. Still pale. No murmurs over the heart and the apex beat was now in the nipple line. Patient had continuted to take Blaud's pill up to time of reporting.

Discussion.

A case where the degree of pallor was much greater than one would expect with blood counts practically normal in all respects. In view of the systolic murmur at the mitral area the presence of some primary disease of the myocardium might be inferred, more/

more so since there was no corresponding mucmur at the pulmonary area which is relatively much more common in anaemia.

No alteration in the blood findings was effected by the giving of iron in the form of Blaud's pill.

Result.

In so far as the anaemia is concerned no improvement was brought about.

Case No.10. D.M. Female Aet 2 yrs.

Complaint. Marked pallor and weakness so that she was unable to walk, also irritability.
The family history was negative for tuberculosis and syphilis.
Previous history was of interest. The patient was a twin born at 7½ mths. and weighed only 4 lbs at birth. The children were breast fed and developed normally, gaining on an average ¼ lb per week.
Present Illness.

At the age of 16 months the patient began to fall behind, became paler, more listless and at the same time very irritable. There was no digestive upset or diarrhoea. The children had been carefully looked after and properly fed. She was given a course of sunlight from Oct. 1927 to Dec. 1927, with only very slight improvement.

Since/

Since Christmas 1927 the pallor has become more marked and the child did not start to walk. Her teeth appeared at the normal times. She has a good appetite and the bowels move regularly once daily. No abnormal odour or constituent has been noted in the stools. The child sleeps well.

On physical examination the waxy creamy pallor was the most striking feature, with a suggestion of a greenish tint under the eyes. The child was bright mentally but resented handling. In the circulatory system the only changes noted were marked acceleration of the pulse rate (140) and displacement of the apex beat outwards $\frac{1}{2}$ in. to the left of the nipple line. The spleen and lymph glands were not enlarged. The liver was palpable about one finger's breadth below the costal margin. Altogether a normal child except for the marked pallor and the rapid pulse. The child weighed 23 lbs. (Normal average aet 2 yrs $25\frac{1}{2}$ lbs.)
Tuberculin (von Pirquet) test was negative.

Stools were examined for occult blood after two days preparation on an iron free diet. The Benzidin test was negative.

There had never been any rash or spontaneous bleedings.

Blood/

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M	NRs.
1	4.4.28	2,220,000	9,300	30	.67	43	36	10.5	1	1.5	4.5	3.5	-
2	7.4.28	2,440,000	15,150	30	.62	55	30	8.5	1	.5	2	3	-
3	14.4.28	3,060,000	17,950	30	.50	52	27	9	3.5	1.5	3.5	3.5	6
4	3.5.28	2,810,000	13,040	35	.62	35	51	7	3	.5	1.5	2	2
5	23.5.28	2,490,000	9,450 (Transfusion)	30	.62	35	47	9	3	1	2	3	1
6	24.5.28	2,650,000	32,000	35	.67	84	9	2	1	-	2	2	-
7	31.5.28	3,090,000	15,550	35	.58	42	42	8	2.5	.5	1.5	3.5	1
8	7.6.28	3,450,000	11,640	45	.66	42	40	9	2	1.5	2	3.5	-
9	14.6.28	3,560,000	10,200	45	.64	27	51	11	4	-	3	4	-
10	28.6.28	4,030,000	13,140	50	.62	40	38	11	2	-	3	6	-

Films.

1. Marked achromia of the red cells which showed as mere rings. Marked anisocytosis and poikilocytosis present. A few macrocytes and very numerous microcytes but no nucleated red cells were found. The Schilling Index gave practically normal readings.

Myelocytes	- per cent	) Total neutrophil
Young metamyelocytes	1 " "	) leucocytes 42
Band forms	4 " "	) per cent.
Polymorphonuclears	37 " "	)

Nothing abnormal was found in the staining of the white cells or in the character of their cytoplasm.

2. The film was very similar to No.1. There was a slight alteration in the white cells an increase in number while the immature forms were fewer.

3. The red cells showed the same changes as in Nos. 1 and 2. Several nucleated reds were found. The Schilling Index.

Myelocytes/

Myelocytes	-	per cent)	Total neutrophil
Young metamyelocytes	1	" ")	
Metamyelocytes	4	" ")	leucocytes 55
Polymorphonuclears	50	" ")	
			per cent.

4. Marked achromia of red cells present, anisocytosis and poikilocytosis also marked. No polychromasia. Two normoblasts found.

"Schilling Index"

Myelocytes	1	per cent)	Total neutrophil
Metamyelocytes	4	" ")	leucocytes 35
Polymorphs	30	" ")	per cent.

5. Blood picture similar to above.

(Transfusion, 200 ccs. citrated blood from father)

6. Very numerous leucocytes were present in the film. A number of deeply staining red cells were found, quite regular in outline and all of practically the same diameter, presumably the corpuscles introduced at the transfusion. In addition there was anisocytosis, poikilocytosis and achromia of other cells.

Schilling Index.

Myelocytes	1	per cent)	Total neutrophil
Metamyelocytes	16	" ")	leucocytes 84
Polymorphs	76	" ")	per cent.

7. Donor's corpuscles still distinguishable. Some pale macrocytes and microcytes present. No polychromasia. One normoblast found.

Schilling Index.

Myelocytes	-	per cent)	Total neutrophil
Metamyelocytes	5	" ")	leucocytes 42
Polymorphs	37	)	per cent.

8./

8. Slight anisocytosis and poikilocytosis present. Red cells were pale, no polychromasia. No nucleated reds found.

Schilling Index.

Myelocytes	-	) Total neutrophil
Metamyelocytes	5	) leucocytes 45
Polymorphs	40	) per cent.

9. Some anisocytosis and achromia but no poikilocytosis present. No nucleated reds found.

Schilling Index.

Myelocytes	-	) Total neutrophil
Metamyelocytes	4	) leucocytes 27
Polymorphs	23	) per cent.

10. Slight achromia present. A few microcytes found. No nucleated reds found.

Diagnosis.

To establish a diagnosis in this case was extremely difficult. The age of the patient and the fact that she was one of twins pointed to Von Jaksch's anaemia as the diagnosis but against this were the complete absence of splenomegaly and the absence of normoblasts and myelocytes in the films.

In view of the very marked lowering of the red cell count and the age of the patient, chlorosis was unlikely as a diagnosis.

The leukaemias were ruled out after examination of the films; there was not a sufficiently marked increase/

increase in lymphocytes to suggest chronic lymphatic leukaemia and too few immature polymorphs and myelocytes to suggest chronic myelogenous; further there was no splenomegaly and no enlargement of lymph glands.

The findings in this case correspond closely with those described by Morse in his Second Type of severe secondary anaemia due to toxaemia (Clinical Pediatrics, p. 620).

In this case no focus of toxaemia could be found.

Treatment and progress.

After the initial period of milk diet necessary for the examination of the stools, the child was given an ordinary mixed diet containing green vegetables, liver, milk, butter, eggs and meat. The child was kept strictly in bed.

7.4.28. was put on liver extract "Hepatex" (Evans and Webb.) drams I t.i.d. equivalent to 24 ozs fresh liver per diem. The child tolerated this extract very well. Pulse rate 140.

14.4.28. Taking her diet very well, still very pale. Pulse 124.

3.5.28. General health was improved. Her mother noticed that the child had become more active and that the limbs felt firmer to the touch.

"Hepatex" discontinued. No haemic murmurs were found. Pulse rate 124.

23.5.28./

23.5.28 Child was still very pale with pink flush over the malar regions. Had taken her food well. Blood transfused from father by the citrate method. About 200 ccs. were given.

24.5.28. No reaction followed the transfusion. Pulse rate rose to about 150. Colour etc. were unaltered.

31.5.28. Child had improved very markedly in general health, was much brighter and her colour was less pale. On examination haemic murmurs were found.

Pulse rate 118.

7.6.28. Still pale, a soft systolic bruit heard over the pulmonary area. Pulse rate 110.

14.6.28. Progress maintained. Murmur present.

28.6.28. Colour much less pale, had taken her food very well and was able to walk again. Murmur was heard at the pulmonary area.

Weight was practically unaltered during the period of obaervation.

Discussion.

A particularly interesting case in view of the negative nature of the clinical findings and the severe degree of anaemia also from the very definite response to a single small transfusion.

Prior to the blood transfusion, the blood findings pointed to a quiescent state of the marrow with almost complete/

complete absence of signs of regeneration in the blood and a normal Schilling Index in the presence of a considerable leucocytosis.

After the transfusion signs of active regeneration appeared in the films and there was a decided "shift to the left" of the Schilling Index.

Another point of interest was the extremely high leucocytosis following the blood transfusion, a proof of stimulation of the marrow by transfused blood.

The alteration in the child's corpuscles were so marked that after the transfusion the transfused corpuscles were easily distinguished for 14 days.

Result.

Considerable improvement.

Case No.11. A.D.K. Male Aet 1½ yrs.

Complaint. Child had never "picked up" after an attack of bronchitis in December 1927, was very thin and pale, had a troublesome loose cough and was very constipated.

Family history was negative for tuberculosis.

Previous history, a premature twin born at the 7th month. The child did well up to the 9th month when he had herniotomy done. Since the operation had a cough/

cough which merged into a definite bronchitis in December (aet 1 yr).

Present illness dated from the attack of bronchitis and at first was only a failure to overcome the results of the bronchitis, such as loss of appetite, persistent cough and loss of weight.

During the 5 weeks prior to admission he lost 2 lbs, became very pale and listless. Both children have shown a somewhat sallow, yellowish colouration of the skin since birth.

Examination showed a very emaciated little boy who lay almost invariably on his left side, who had noisy grunting respiration. The facies was distinctly yellow but there was no evidence of icterus in the sclera. Marked pallor of the lips, tongue and conjunctivae.

Systems. Respiratory. Inspection, marked diminution of movement on left side. Rate 44.

Cough is loose and infrequent, no expectoration.

Auscultation, high pitched bronchial breathing all over the left side with increased vocal resonance. Percussion, impaired note all over the left side.

Circulatory. Apex beat visible in 5th space ½ in. to left of the nipple line.

Pulse/

Pulse rapid and fine 146.

Auscultation, soft, systolic murmurs at the mitral and pulmonary areas.

Alimentary. Slight fullness of the abdomen.

Palpation, a few hard masses felt just above the symphysis and the edge of the liver about two fingers breadth below the costal margin. The spleen was not palpable.

Nervous. The child was very listless and apathetic. Fontanelle sunken.

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	15.5.28	2,240,000	18,080	25	.57	52	36	5	1.5	-	2.5	3
2	23.5.28	2,160,000	15,640	25	.59	42	45	6	2	-	2	3
3	30.5.28	2,120,000	11,740	25	.59	39	54	4	.5	-	1	1.5

Films.

1. Marked achromia but no polychromasia present. Marked poikilocytosis and anisocytosis with numerous macrocytes but no nucleated red cells discovered.

Schilling Index.

Myelocytes	-)	
Young metamyelocytes	1)	Total neutrophil
Metamyelocytes	7)	leucocutes 52
Polymorphonuclears	44)	per cent.

2. Very similar to No.1 but 4 normoblasts were seen.

3. Red cells similar to the above but quite frequent nucleated cells, 22 normoblasts and 2 megaloblasts.

Schilling/

Schilling Index.

Myelocytes	1)	Total neutrophil
Young metamyelocytes	3)	leucocytes 39
Metamyelocytes	25)	per cent.
Polymorphonuclears	10)	

Diagnosis.

Delayed resolution following bronchitis and probably broncho-pneumonia, carnification of the left lung.

Treatment and progress.

X-ray examination confirmed the presence of consolidation of the whole of the left lung, no air containing tissue was demonstrated. Exploration excluded pleuritic effusion as the cause of the shadow. General treatment was given with the addition of Syr. ferri. phos. co. drams I t.i.d. and malt in similar doses.
The child did not respond to treatment and died on 30.5.28 within two hours of taking the third blood count.

Post-mortem.

Body very emaciated. The pericardium was adherent to the posterior surface of the sternum and in separating these adhesions a large quantity of greenish pus welled up. The pericardium was markedly thickened and the inner surface was covered by a shaggy layer of fibrinous lymph. The left lung was collapsed and firmly/

firmly bound down by old standing adhesions to the lateral and posterior walls of the thorax. When a portion of this lung was removed and cut into, the section closely resembled pale muscle, e.g., heart muscle. The right lung was healthy.

The liver was enlarged and had a somewhat "nutmeg" appearance.

The spleen was not enlarged and nothing else abnormal was found.

The pus contained numerous Gram positive diplococci, pneumococci.

Sections. Lung showed evidences of chronic bronchopneumonia. There were evidences that the inflammatory changes and fibrosis were still continuing.

Liver showed evidences of chronic passive congestion, atrophy of the centre of the lobules and deposits of fat in the cells at the periphery.

Spleen showed evidences of passive congestion.

Discussion.

Quite apart from the well marked anaemia due to absorption of toxins from the infection of the pericardium, the case was very interesting firstly because the apex beat was visible throughout the illness in practically the normal position. The writer/

writer observed this particularly on the 30th May within a few hours of the child's death.

A second point of interest was the absence of febrile reaction.

Thirdly the gradual diminition in the leucocyte count pointing to an overwhelming toxaemia while at the same time nucleated red cells appeared in the films and continued to increase in number up to time of death.

There was a marked increase in immature leucocytes before death also pointing to a massive toxaemia.

Result.

Death from toxaemia plus respiratory embarrassment due to collapse of the left lung.

Case No.12. F.H. Male Aet 8 yrs.

Complaint: Nose bleeding of severe degree on day of admission. A tendency to bruising and discolouration of the skin from slight causes.

Family history revealed the presence of a tendency to bleed easily in a brother aet 4 yrs. but no such tendency in any maternal uncle or male relative on the mother's side.

Previous history.

A full time child, delivered naturally, there was no bleeding at the time of separation of the cord or during/

during the whole period of infancy. The first indication that any abnormal tendency to bleeding existed in the patient was at the age of three years when he was circumcised. Bleeding at the operation was not particularly noticable but the dressings became soaked with blood in a short time. Every effort was made to stop the oozing but in spite of everything it continued for six days by which time the child was almost exsanguinated and very ill. Recovered slowly and continued in fairly good health up to the age of six years when during an attack of measles he vomited a quantity of blood. A year ago he was in hospital with prolonged bleeding from a cut finger.

Present illness. 29.5.28. Received a blow on the face which caused epistaxis; bleeding continued for about 15 mins. The same evening recurrence of epistaxis which continued for an hour. The following afternoon while still in bed had further bleeding which again lasted for about an hour. About 11.30 p.m. he vomited a quantity of clotted blood. Admitted to hospital 31.5.28.

Examination.

A very pale boy with a somewhat swarthy complexion. The lips, tongue, and conjunctivae were pale.
No epistaxis on admission.

Systems/

Systems.

Circulatory. Pulse rapid and fine, rate 106.

Heart. Apex beat visible just below the nipple, no enlargement of the heart.

Respiratory, nothing abnormal detected.

Haemopoietic, no enlargement of the spleen on percussion. No palpable lymph glands.

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1.	1.6.28	4,250,000	8,300	60	.71	55	28	8	3	.5	2.5	3
2	5.6.28	3,350,000	6,080	50	.75	61	22	7	2	1.5	3.5	3
3	6.6.28	3,080,000	9,300	50	.83	68	17	5	3	.5	2.5	4
4	8.6.28	3,460,000	10700	55	.80	74	16	4	1	-	3	2
5	10.6.28	3,340,000	7,050	50	.75	63	20	10	2	-	3	2
6	15.6.28	3,530,000	8,200	55	.78	62	27	5	2	-	2	2
7	22.6.28	3,850,000	8,480	55	.71	58	28	6	2	-	3	3

Films.

1. Both red and white cells were normal.

2. Similar findings to above.

3. A slight degree of anisocytosis and achromia were present and a few poikilocytes were found. No nucleated red cells were found.

4. A few macrocytes and poikilocytes were found also two polychromatic cells.

5. Slight anisocytosis and poikilocytosis, no nucleated red cells found.

6. Slight achromia and anisocytosis, no nucleated red cells found.

7. Slight anisocytosis was the only abnormality present in the red cells.

Coagulation/

Coagulation time.

This was estimated by the capillary tube method, i.e., the tube containing about 1 inch of blood was tilted every half minute and the time noticed when the column of blood ceased to flow.

Normal controls 4½ and 6½ mins.

Date.	Coag-time.	
1.6.28	14 mins.	
5.6.28	7 mins.	(Calcium lactate grs V t.i.d.
6.6.28	9½ mins	commenced)
8.6.28	8 mins.	
10.6.28	7 mins.	
15.6.28	8½ mins.	
22.6.28	7 mins.	

Diagnosis. Haemophilia.

Treatment and Progress.

As there was no recurrence of the nose bleeding after the 1st June the patient was allowed to go home although the coagulation time was 14 mins.
On his readmission on the 5th the signs of anaemia were well marked; soft systolic murmurs were heard at the pulmonary and mitral areas and the boy was very pale. A loud venous bruit was heard over the jugular opening.

Apart from a very slight epistaxis of the 6th there was no further bleeding. On the 8th he had a slight rise of temperature accompanied by nasal catarrh. These continued for two days when a crop of vesicles typical of chicken-pox made their appearance.

No/

No bleeding at the separation of the crusts.
Treatment consisted in nasal packs of gauze wrung out in adrenalin for 24 hrs. followed by the administration of calcium lactate grs. V t.i.d.

Discussion.

A case of anaemia due to loss of blood following injury in a haemophiliac.

There were no outstanding peculiarities in the blood films.

The coagulation times were interesting in that the high reading on 1.6.28 was so soon followed by a further bleeding and in that no bleeding occurred after 5.6.28 when the coagulation time was 7 mins.
In view of the subsequent history of the case it would appear that it is inadvisable to allow a haemophiliac to be up when the coagulation time is prolonged.

There was an increase of leucocytes at onset of the attack of chickenpox with a marked increase in neutrophil polymorphs.

Result.

Partial recovery from anaemia of moderate severity. Prognosis very uncertain.

Case No.13/

Case No.13. W.B. M. Aet 2 yrs.

Complaint. Inability to walk, had choking fits and had become pale during 6 weeks prior to admission.

Family history was negative.

Previous History.

A full time child weighing 8½ lbs at birth, the patient developed normally up to the age of 10 months when he had a "fit" coincident with the eruption of his 1st tooth.

Had measles aet 1½ yrs.

Present Illness.

Six weeks prior to admission began to have "crowing fits", became "blue in the face" about 3-8 times per day and clenched his fists. "His flesh became soft" and he sweated profusely at night. His mother noticed abnormal motility at the wrists.

Examination

Examination showed all the physical signs of rickets associated with laryngmus stridulus and tetany. The fontanelle was open and there was marked swelling of the epiphyses.

Circulatory system. No haemic murmurs were heard.

Haematopoietic system. No enlargement of the spleen detected.

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	10.3.28	3,920,000	9,400	60	.76	45	33	15	2	-	2.5	2.5
2	24.3.28	4,130,000	10950	60	.68	47	29	12	4	-	5	3

Films.

1. There was considerable achromia of the red cells with irregularity in size. No changes were noted in the white cells.

2. Slight achromia and anisocytosis were the only abnormalities present.

Diagnosis. Florid rickets.

Treatment and progress.

10.3.28. Child given cod liver oil ℥I t.i.d. and a generous diet. A course of artificial sunlight was commenced.

24.3.28. Allowed to go home. No spasms were noted after three days. The patient's general condition on discharge was slightly improved but manifestations of rickets still very evident.

The child did not continue with treatment and so further counts were not made.

Discussion.

A typical case of rickets with a mild degree of anaemia which showed commencing improvement after 14 days hospital treatment.

Result.

Slight improvement.

Case No.14./

Case No.14. E.M. F. Aet 2½ yrs.

Complaint. Inability to sit up, general backwardness, failure to develop normally.

Family History was negative.

Previous History. A full time child, delivered normally. The patient developed normally up to the age of 4 months.

Present Illness.

At the age of 4 months swelling and protrusion of the abdomen were noted, also the skin became of a pale yellowish tint. The child was noticed to be very heavy and inattentive and did not smile in the usual way. The skin became coarse, dry and cold to the touch.

She has never been able to sit unsupported and cannot walk or speak. She cut her first tooth at the age of 2 yrs 2 mths.

Examination.

Examination showed the typical facies of the cretin with the heavy expression, open mouth and protruding tongue; the yellow skin and thickening of the edge of the eyelids.

Abdominal protrusion was of moderate amount. No abnormal physical signs were detected in the heart or lungs and no enlargement of any abdominal organ.

Weight 16 lbs. Height 25 ins.

(Normal 25 lbs. Height 28 ins.)

Blood/

Blood count.

	R.B.Cs	W.B.Cs	Hb.	CI	P	SL	LL	E	B	T	M
21.6.28	3,230,000	12,360	50	.78	32	50	9	2	.5	2.5	4

Films showed slight anisocytosis and achromasia of red cells.

White cells showed no abnormalities.

Diagnosis. Hypothyreoidism.

Treatment and Progress.

The child had been on thyreoid tablets grs. $\frac{1}{10}$ daily for some 9 or 10 months prior to coming to hospital.

Dose increased to grs $\frac{1}{2}$ t.i.d.

Child was not brought back to report.

Discussion.

A moderate degree of anaemia occurring as part of the general underdevelopment.

There was a relative lymphocytosis showing that the bone marrow was not forming the normal number of cells.

Result. In statuo quo.

Case No.15. J.R. Male. Aet $2\frac{10}{12}$ yrs.

Complaint. The child was brought to hospital because of a number of large bruises which had/

had appeared on his legs and trunk without any history of a blow over these regions.

Family History was negative with regard to a tendency to bleeding or bruising in any of the males.

Previous History.

The patient had been healthy since infancy.

He had measles, aet 10 mths. and mumps aet 1 yr 4 mths.

Present Illness.

On 24.5.28 the patient's mother noticed a large discoloured area in the right groin and two smaller areas on front of left leg.

On 25.5.28 she noticed a further bruise on left elbow.

Examination.

A healthy bright little boy with good colour. Bruises were present in the areas stated in the history, all subcutaneous.

A fine purpuric rash was present on the abdomen and legs.

Haematopoietic system.

The spleen was not enlarged.

Blood counts.

		R.B.Cs	W.B.Cs	Hb	CI	P	SL	LL	E	B	T	M
1	26.5.28	4,390,000	8,760	55	.63	20	58	12	3.5	-	5	6
2	7.6.28	4,360,000	10,400	55	.63	28	54	11	1	-	3	3

Film/

Films 1. A few microcytes were found. White cells normal.

2. Red and white cells were normal.

Bleeding time. 26.5.28 7½ mins.

7.6.28 6 mins.

Diagnosis. Purpura Haemorrhagica.

Treatment and progress.

After admission there was no spread of the rash and no further bruises appeared.

The rash gradually faded during the four or five days after admission. The bruises were still visible but of lessened area at time of discharge.

Patient was given calcium lactate grs. V t.i.d. during his stay in hospital.

Discussion.

A case of very mild anaemia due to blood loss by effusions under the skin. The only point of interest in the blood counts was the leucocytosis with increase of polymorphs in count No.2.

Result.

Recovery.

SECTION VIII.

GENERAL DISCUSSION.

In this section the nature of the various clinical manifestations and their value in diagnosis are discussed.

PALLOR is the outstanding clinical manifestation of anaemia.

The colour of the skin and accessible mucous membranes depends on a number of factors, the chief being the haemoglobin of the red blood corpuscles. The size and nearness to the surface of the capillaries in the skin and the efficiency of the circulation through them are factors altering the colour of the skin.[66]

Deficiency of haemoglobin and inefficiency of the circulation, e.g. in diphtheria with myocarditis cause pallor.

The amount of pigment in the skin varies, being greater in dark haired subjects. An increase of pigment masks the pallor of anaemia.

The skin varies in thickness, an increase rendering it paler as in myxoedema.

In older children the pallor may be the result of nervous action on the cutaneous blood vessels. Some children become pale under any strong emotion, an angio-neurosis.[67]

The/

The various areas commonly used in estimating pallor are the facies, the conjunctivae, the lips, the tongue and finger nails. Of these areas the lips are perhaps the most reliable for the area is fairly large, they are unlikely to be the seat of any inflammatory changes which so readily alter the conjunctivae, they are uninfluenced by the hereditary factors which affect the facies as a whole and are uninfluenced by the effect of gravity which alters the colour of the nails. Furring of the tongue detracts from its value in estimating pallor.

Feebleness of the cardiac musculature may influence the value of all the areas mentioned.

The presence of the lesser degrees of pallor are therefore of little help in estimating the degree of anaemia.

Case No.9 showed a moderate degree of pallor while the blood counts were practically normal for her age. The presence of cardiac weakness as the cause of the pallor in this case was suggested by the finding of a mitral systolic murmur while no murmur was heard at the pulmonary area. In anaemia the murmur at the pulmonary area usually appears before that at the mitral area.

MANIFESTATIONS/

MANIFESTATIONS IN THE CIRCULATORY SYSTEM.

ACCELERATION OF THE PULSE RATE AND LOWERING OF THE BLOOD PRESSURE.

In anaemia the decrease in the number of red cells and percentage haemoglobin reduces the oxygen-carrying capacity and leads to retention of waste products in the tissues.

The physiological response to oxygen "want" and carbon dioxide excess is acceleration of the heart rate. The heart muscle itself is no longer supplied with a sufficiency of oxygen and there is as a direct result muscular weakness and failure to maintain the normal blood pressure.

HAEMIC MURMURS.

Murmurs are heard over the heart when from any cause there is narrowing of an orifice or an alteration in the relative diameters of the cavities through which the blood flows. Deficient oxygen supply leads to weakness of the cardiac musculature and a diminution in tone of the larger blood vessels.

Dilatation of the pulmonary artery is the most probable cause of the haemic murmur.

Alteration in the blood itself with a lowering of the viscosity may be a factor in the production of such murmurs.

Haemic/

Haemic murmurs are not constantly heard in cases of anaemia.

In the series of 15 cases the writer found murmurs present in 4.

Murmurs tend to appear in anaemias of moderate severity, i.e. when the red cell count drops to 2½ or 3 millions with haemoglobin 30 or 40 per cent.

The occurrence or perhaps more correctly the detection of haemic murmurs is influenced by the heart rate irrespective of the degree of anaemia. With an acceleration of the heart rate murmurs tend to disappear.

Case No.3 with a red cell count of 3,150,000 had no haemic murmurs, the pulse being rapid, about 150. 11 days later a murmur was heard, the pulse having dropped to 90 and the red cell count to 2,810,000 which in itself is too small a drop to bring about any striking alteration in the physical characteristics of the blood.

Case No.10 with very severe anaemia had no haemic murmurs while the pulse rate was 140.

Haemic murmurs are less frequent in children than in adults.[68] The finding of a soft blowing systolic murmur at the pulmonary area in a patient who is pale would indicate that the pallor is due to anaemia rather than to any of the other causes mentioned above.

Haemic/

Haemic murmurs also occur in patients who are not anaemic. Landis and Kaufman found murmurs in 84 out of 99 cases.[69]

VENOUS HUM.

A sign which is somewhat indeterminate and difficult to identify clinically, is due to vibrations set up by the flow of blood, of lowered viscosity through the rigid opening in the fascia where the external jugular vein passes into the deeper planes of the neck.

COLDNESS OF THE EXTREMITIES.

This is an indication of cardiac inefficiency.

ENLARGEMENT OF THE SPLEEN.

This is stated to be a frequent accompaniment of anaemia in children but in the series of cases there was palpable enlargement in one case only:- No.5. When enlargement of the spleen occurs it may be explained in the majority of cases, in all those due to bacterial action, as a hyperplasia to deal with the increased number of damaged blood cells in the circulation.

In infants with severe anaemia enlargement of the spleen may be due to that organ taking up again its foetal function of blood formation.

The absence of enlargement in some severe cases of anaemia is difficult to explain, e.g. Case 10. Perhaps/

Perhaps in these cases the amount of haemoglobin to be dealt with is relatively small and within the compass of the normal spleen.

In special diseases, e.g. Gaucher's disease, the enlargement is due to hyperplasia of special cells and no adequate reasons for these changes have been found.

The finding of an enlarged spleen in a case of anaemia is not as a rule of much assistance in arriving at a diagnosis and is of no value in forming an estimate of the severity of the anaemia.

ENLARGEMENT OF LYMPH GLANDS.

When this occurs it is due to the causal infection in anaemias from bacterial causes. In the neoplastic types of anaemia it is due either to hyperplasia of one special cell, e.g., Hodgkin's disease, or to growth of abnormal cells of metastatic origin, e.g., myelogenous leukaemia.

Enlargement of lymph glands may also be due to malnutrition.[70]

CAUSATION.

Anaemia has been shown to arise from a great variety of causes which act in one of three ways:-

I. By increasing the rate of blood destruction.

II. By inhibiting the blood forming activities of the bone marrow.

III. By a combination of I and II.

The incidence of anaemia is much greater among the poorer classes coincident with the greater prevalence of infective illnesses and malnutrition.

Of all the causes of anaemia bacterial infection and the action of their toxins are the most frequent.

The well defined blood diseases such as purpura and leukaemia are rare while chloroma, Gaucher's disease and Banti's disease are very rare indeed.

Certain causes of anaemia are peculiar to an individual group, e.g. Von Jaksch's and anaemia from rickets in Group II.

TREATMENT.

The value of the various methods of treatment is very difficult to assess. Time and usage give pride of place to iron and arsenic.

Recent investigations, especially on recovery from haemorrhage, seem to show that iron does not exercise the beneficial action commonly attributed to it in increasing and accelerating the formation of haemoglobin. (vide page 88).

Apart from chlorosis in which iron acts almost as a specific the use of the drug cannot be expected to give any striking results in the treatment of anaemia. However its use seems rational and is to be recommended in full doses to obtain any effect. It seems as if

the/

the quantity sufficient for the needs in health, is ineffective or is rendered inactive in some way.

The utility of arsenic is questionable in the treatment of anaemia in children. Apart from the general tonic effect no action on the haematopoietic system has been demonstrated.

Other drugs are of no value in so far as the anaemia itself is concerned.

Blood transfusion affords a rational means of replacing blood loss. In view of the fact that after a small transfusion a remarkable increase in the activity of the haematopoietic tissues takes place, it may be found on further investigation that some substance in the nature of a hormone necessary for the proper activity of these tissues is introduced. This method is of the greatest value in the treatment of anaemia from all causes.

Artificial sunlight has only a very small value in so far as the cure of anaemia is concerned but from its general stimulating action it should be used in all cases which cannot be placed in an "outdoor" environment as a substitute for the deficient natural sunshine.

The use of liver diets and liver extracts in the treatment of anaemia is too recent to arrive at any conclusion as to its real value. All the published results point to this method as being of the utmost value/

value in pernicious anaemia and of considerable value in secondary anaemias.

No change in the blood findings were found in Case No.10 after a course of liver extract.

Treatment by drugs and special methods therefore are of some value but alone cannot bring about a complete cure of the anaemia in the large majority of cases. Reliance must be placed rather in an efficient and careful search for possible causes, thorough removal of these where possible and the placing of the patient in the best possible environment for recovery.

PROGNOSIS.

A prognosis can only be given in any case of anaemia after a careful consideration of the clinical findings and a series of blood examinations. In so far as the blood examinations are concerned, the characteristics of the blood at the various ages must be kept in mind.

The tendency for the blood in early life to revert to an almost foetal type of formation is confusing. The appearance of normoblasts are apt to make the condition appear more serious than it really is.

A steady increase in the number of red cells even if accompanied by a lesser increase of haemoglobin and/

and a lowering of the colour index is of good prognostic significance.

In films the evidences of active regeneration are of good significance. The younger the child, the greater are the evidences of regeneration and the earlier the forms appearing, polychromasia in mild cases, normoblasts in more severe.

The blood count is misleading in only one condition, namely, in cases with marked dehydration from vomiting and diarrhoea. Here the cell counts are maintained at a high level although it is almost certain that the haematopoietic tissue is unable to produce cells at the normal rate.

In examination of films one difficulty is encountered, namely, in aplastic anaemia where the cells are normal in all respects, the counts however help to clear up the difficulty. A determination of the absolute number of the various white cells as suggested by Lucas would be of value as showing, from the number of polymorphs, the state of activity of the bone marrow.

The Schilling index is of great value in showing the state of activity of the bone marrow. In a case with no leucocytosis but an increase in immature forms, i.e. a shift to the left, there is almost certainly a concealed focus of infection and an increased activity of the functions of blood formation and destruction.

The finding of a definite cause and the success or otherwise in removing it will be of great value in giving a prognosis.

In primary Anaemias the prognosis is always doubtful, being best in a typical case of Von Jaksch's anaemia.

In secondary anaemias the prognosis varies with the cause. In cases of leukaemia, chloroma and Hodgkin's disease the prognosis is always very grave.

CONCLUSIONS.

1. That, with the exception of the first two weeks of life, the number of red corpuscles and the percentage of haemoglobin during infancy and childhood are much below the adult figures.

2. That a complete diagnosis in a case of anaemia cannot be made from clinical findings alone and that no estimate of the severity of the condition can be made from these findings.

3. That in the diagnosis of any case of anaemia a complete blood examination must be made and that the prognosis should be based on these findings.

4./

4. That enlargement of the spleen is by no means so frequent an accompaniment of anaemia as would appear from the literature.

5. That the most certain therapeutic method in anaemia is undoubtedly blood transfusion either prior to or after the removal of any source of toxaemia.

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